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Fr m: Ford, Vanessa
Sent: Tuesday, November 18, 2003 12:47 PM
T : STIC-Biotech/ChemLib
Subject: In re: 10/040,830 Journal articles

Please supply the following journal articles:

1. AU Wang A.; Jankovic J.
CS Dr. J. Jankovic, Movement Disorders Clinic, Department of Neurology,
Baylor College of Medicine, 6550 Fannin, Houston, TX 77030, United States
SO **Muscle and Nerve, (1998) 21/12 (1740-1747).**
Refs: 96

12323686

2. U Borodic G.E.; Acquadro M.A.
CS Dr. G.E. Borodic, 100 Charles River Plaza, Boston, MA 02114, United
States. borodic@aol.com
SO **Journal of Pain, (2002) 3/1 (21-27).**
Refs: 27

COMPLETED

3. TI Headache management in an interventional pain practice.
AU Trescot A.M.
CS Dr. A.M. Trescot, 1895 Kingsley Ave., Orange Park, FL 32073, United States
SO **Pain Physician, (2000) 3/2 (197-200).**
Refs: 11

4. TI HEMIFACIAL SPASM - A REVIEW
AU WILKINS R H (Reprint)
CS DUKE UNIV, MED CTR, DIV NEUROSURG, DURHAM, NC, 27710
CYA USA
SO **SURGICAL NEUROLOGY, (1991) Vol. 36, No. 4, pp. 251-277.**

5. U Borodic G E (Reprint); Acquadro M A
CS 100 Charles River Plaza, 3rd Floor, Boston, MA 02114 USA (Reprint);
Harvard Univ, Massachusetts Gen Hosp, Sch Med, Dept Anesthesia & Crit
Care, Boston, MA USA; Harvard Univ, Massachusetts Eye & Ear Infirm, Sch
Med, Dept Ophthalmol, Boston, MA USA
CYA USA
SO **JOURNAL OF PAIN, (FEB 2002) Vol. 3, No. 1, pp. 21-27.**

6. TI Use of botulinum toxin to alleviate facial
pain.
AU Girdler N M
SO **BRITISH JOURNAL OF HOSPITAL MEDICINE, (1994 Oct 5-18) 52 (7) 363.**
Journal code: 0171545. ISSN: 0007-1064.

Hemifacial Spasm: A Review

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Wilkins RH. Hemifacial spasm: a review. Surg Neurol 1991;36:251-77.

Hemifacial spasm can be diagnosed by observation and clinical history. It is thought to arise primarily from compression of the facial nerve at the pons, usually by an adjacent artery. Although many approaches to treatment have been tried, the most effective is microvascular decompression of the facial nerve at the pons. That operation has well-recognized risks, including ipsilateral deafness. The latter complication ordinarily can be avoided by the use of intraoperative monitoring of auditory evoked potentials.

KEY WORDS: Hemifacial spasm; Microvascular decompression

Diagnosis and Differential Diagnosis

There are many types of abnormal spontaneous facial movement (Table 1). Blair and Berry [27] have listed ten, the first seven of which are:

1. Hemifacial spasm
2. Essential blepharospasm
3. Facial myokymia
4. Habit spasm (tic)
5. Focal cortical seizures involving facial muscles
6. Aberrant nerve regeneration after injury or Bell's palsy
7. Tardive dyskinesia

To these may be added several other categories such as Meige's syndrome (blepharospasm plus oromandibular dystonia) [338], wincing in response to the pain of tic douloureux [355], masticatory spasm in facial hemiatrophy [161], and focal facial spasm [255]. An entire listing of cranial-cervical dyskinesias includes many more types [126,129], but these are not likely to be confused with hemifacial spasm.

Goldstein [100] has emphasized the importance of

direct observation in establishing the true nature of a facial movement disorder: "In the game of bridge, there is the old expression that 'one peck is worth two finesses.' In the field of neurology, it is equally true that one look at aberrant movements of the face or limbs is much more helpful than a written description."

Hemifacial Spasm

Hemifacial spasm (HFS) is a syndrome of spontaneous and gradual onset that has as its hallmark the intermittent twitching of the muscles of facial expression on one side of the face [5,62,71,156,177,346,352]. Typical HFS begins about the eye and later spreads to involve other muscles innervated by the ipsilateral facial nerve, including at times the platysma. Some individuals (eg, 7.4% of 366 patients reported by Jannetta) have atypical HFS, which begins in the buccal muscles and progresses upward over the face [134,139]. With either form of intermittent muscle spasms, tonic muscular contractions may appear as well. Characteristically, a series of twitches, increasing in frequency and intensity, is followed by a sustained spasm. The paroxysms of facial contraction are not accompanied by lacrimation or nasal discharge, and they are not followed by a refractory period [93]. Voluntary facial movement may trigger the involuntary contractions of HFS, and an effort to relax the face may result in momentary and slight diminution of spasm. HFS is frequently intensified by fatigue, stress, anxiety, or self-consciousness. At times, its severity may be altered by a change in head and body position [139]. It may persist during sleep [71,233]. After the condition has been present for some time, mild ipsilateral facial weakness may develop.

In 1967, Diamant et al [61] reported that in two patients with HFS, contractions of the stapedius muscle occurred in synchrony with the facial twitches. More recently, Kim and Fukushima [168,169] noted that patients with HFS frequently complain of a peculiar type of ipsilateral tinnitus: a low-pitched noise perceived synchronously with spasm or voluntary contraction of the facial muscles. Among 47 of their patients, 15 complained of such tympanic noise. Impedance audiometry in the 47 cases showed spasm or synkinesis of the stape-

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Table 1. *Clinical Differentiation of Hemifacial Spasm from Other Disorders of Facial Movement*

	Sex	Age	Side	Voluntary control	Sleep	Clinical characteristics	Association	Electrophysiologic testing
Hemifacial spasm	F > M	50-70	Unilateral	No	May be present	Tonic/clonic movement of facial muscles innervated by seventh cranial nerve	Vessel compressing on seventh cranial nerve root at entry zone (dolichoectatic vessel) Tumor AVM	Blink reflex latency normal; usually synkinetic movement with appearance of response in muscles other than orbicularis oculi on the affected side EMG: Arrhythmic discharge, 20-40/sec
Blepharospasm	M = F	50-70	Bilateral	Yes (somewhat)	Absent	Bilateral synchronous spasms of the orbicularis oculi	Midbrain and thalamic infarcts Progressive supranuclear palsy Meige's syndrome	Blink reflex latency normal. May see increased amplitude; no synkinesis EMG: facial muscles normal voluntary motor units
Orofacial dystonia (Meige's syndrome)	M = F	Any age	Bilateral	No	Absent	Writhing movements often involving the tongue and respiration	Drugs Basal ganglia disease	Blink reflex normal EMG: normal
Facial synkinesis after Bell's palsy	M = F	Any age	Unilateral	No	Present	Unilateral facial weakness; may see "crocodile tears," gustatory lacrimation	Prior history of facial paralysis	Blink reflex: increased latencies of R1 and R2 on the affected side EMG: evidence of synkinesis and fibrillation potentials and reduced motor units
Spastic paretic facial contracture	M = F	Any age	Unilateral	No	Present	Hemifacial smile present at all times but paretic on voluntary movement	Brain stem glioma Multiple sclerosis	Blink reflex: may see increased latencies of R1 and R2 on the affected side

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Spastic parietic facial contracture	M = F	Any age	Unilateral	No	Present	Hemifacial smile present at all times but parietic on voluntary movement	Brain stem glioma Multiple sclerosis	Blink reflex: may see increased latencies of R1 and R2 on the affected side EMG: fibrillation potentials and reduced number of motor units. Myokymia may be seen
Facial myokymia	M = F	Any age	Unilateral (rarely bilateral)	No	Present	Constant, rapid undulation and flickering muscles ("bag of worms appearance")	Multiple sclerosis Intramedullary tumor	Blink reflex latency normal EMG: myokymic discharge (grouped fasciculations)
Facial tic	M = F	Children	Bilateral or unilateral	Yes	Present	Stereotypic movements: brief, repetitive, suppressible	Gille de la Tourette's syndrome	Blink reflex latency normal EMG: normal (usually)
Focal seizure of the face	M = F	Any age	Unilateral	No	—	Movements occurring with head and eye deviation	Focal cortical lesion	Blink reflex latency normal EMG: normal EEG: abnormal

Source: Digre and Corbett, in *Advances in Neurology*, "Hemifacial spasm: Differential diagnosis, mechanism, and treatment," 1988.

Abbreviations: AVM, arteriovenous malformation; EEG, electroencephalogram; EMG, electromyogram.

dius muscle on the affected side in 41 (87%). Parenthetically, Kim and Fukushima found that both the subjective and objective aspects of stapedius involvement were ordinarily relieved by the same surgical procedure (microvascular decompression of the facial nerve at the brain stem) that relieved the HFS.

HFS occurs almost exclusively in adults [157,185, 290,318]. Although familial cases have been described [41,85,99,197], HFS is ordinarily not a hereditary disorder. It affects women more often than men. For example, among 106 patients reported by Ehni and Woltman [71], 64 were female and 42 were male; and among 366 patients reported by Jannetta [134], 243 were female and 123 were male. In a recent epidemiological study, Auger and Whisnant [18] found the average prevalence rate of HFS to be 14.5 per 100,000 in women and 7.4 per 100,000 in men. The ages of onset in the series of Ehni and Woltman [71] ranged from 17 to 70 years with a mean age of 45 years; in Jannetta's series [134], the age range at presentation was 13 to 77 years (average, 51 years) with a mean duration of symptoms of 8 years.

In the latter series, the left side of the face was involved more often than the right (214:152), with only four patients demonstrating bilateral HFS [134]. In contrast, Ehni and Woltman [71] found in analyzing their patients that in neither sex was one side of the face affected more often than the other. Six patients, five of them women, had bilateral HFS. The interval between the onset on one side and the onset on the other varied from less than a year to 15 years; in no patient were the spasms synchronous or symmetric.

Of 74 patients with HFS whom I have treated personally, all were adults. Of these, 57 (77%) were women and 17 (23%) were men. The abnormal movement was on the left in 42 (57%) and right in 32 (43%).

HFS primarily presents a problem of appearance for the affected individual, but when it becomes marked, it interferes with binocular vision and thus with activities such as reading and driving. It fluctuates in severity, but generally becomes more pronounced with time. Among the 106 patients reported by Ehni and Woltman [71], nine experienced one or more periods of complete freedom from spasms, lasting from a few weeks to 3 years. However, HFS ordinarily does not resolve permanently or for long periods without treatment.

The key to the diagnosis of HFS is the clinical observation of the abnormal facial movements. The electromyogram (EMG) may also provide useful diagnostic information [156]. Esslen [76] has stated that HFS is one of the rare conditions with a truly pathognomonic discharge pattern on EMG.

Hjorth and Willison [116] studied 10 patients with HFS by electromyography and found two types of ab-

normal movements. The first consisted of brief, rapid twitches that occurred simultaneously in several facial muscles, often in association with blinking. Such brief twitches were accompanied by a characteristic EMG appearance of isolated bursts of repetitive motor unit discharge at high frequencies. Each burst consisted of 2 to 40 discharges of the same motor unit. The interval between the bursts varied and the firing rate varied both within a burst and from burst to burst. The highest frequency ordinarily fell in the 200-250 Hz range, but was as high as 350-400 Hz. A decrement of motor unit action potentials was often seen during the bursts.

The second, and less common, type of movement encountered by Hjorth and Willison was a prolonged, irregular, fluctuating contraction that caused forced eye closure for several seconds. Although it was not possible in this situation to record single motor units in isolation, the authors could determine that the units fired irregularly with discharge rates much lower than those of the brief twitches.

Magun and Esslen [199], in an electromyographic study of 15 patients with HFS done 14 years earlier, found that the EMG was characterized by rhythmically occurring bursts, usually consisting of 5 to 20 discharges per second. The rate of discharge of these bursts was exceptionally high, up to 150 to 250 per second, a frequency not obtained in the intact contralateral facial musculature. Furthermore, there was almost complete synchronization of the discharges within the ipsilateral facial muscles. With weak innervation, the bursts often fired irregularly during the normal activity of the units, but with increased innervation, such as when smiling or winking, a prolonged spasm frequently occurred that could conceal or replace normal activity. Magun and Esslen also found that there was a surprisingly long latency following electrical stimulation of the involved facial nerve.

Other studies ordinarily are not of help in establishing the diagnosis of HFS, but are valuable in identifying the cause in those relatively few patients with an easily identifiable pathological process such as an ectatic and elongated vertebrobasilar arterial system (megadolichovertebrobasilar anomaly), aneurysm, arteriovenous malformation, or neoplasm. For this reason, before treatment is undertaken, patients with HFS should be studied by computed tomography (CT) or magnetic resonance imaging (MRI) [58,63,322,335]. In general, these modalities are not sufficiently refined to identify the exact neurovascular relationships at the brain stem that are crucial to treatment by microvascular decompression, but they will reveal larger processes such as those mentioned, in which case angiography of the posterior circulation may then be worthwhile for further definition of the abnormality. Although preoperative

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posterior circulation angiography has been utilized extensively in patients with HFS by a few surgeons [19,102,174-176,236,294], most have not and do not obtain angiography on a routine basis, thinking that the discomfort and risks involved outweigh the benefit. Occasionally, other diagnostic studies may be helpful, such as plain roentgenograms and tomograms of the skull base in patients with Paget's disease or other bony abnormalities of the skull base.

From time to time, HFS may be associated with ipsilateral acoustic or trigeminal nerve dysfunction, probably because of a shared etiology such as compression of the involved nerves at their junction with the brain stem [232]. Such dysfunction of the acoustic nerve may be manifested by an ipsilateral reduction in auditory acuity, but tinnitus and vestibular disturbances have also been described [176,231,258]. Among the 106 patients of Ehni and Woltman [71], 15 had impaired hearing on the side involved by spasm, and of 137 patients reported by Møller and Møller [231], the acoustic middle ear reflex was abnormal preoperatively in 56 (41%). However, among the 57 patients of Fukaya and Nomura [87], only 1 had impaired hearing on the affected side.

In 1920, Harvey Cushing [54] used the term "painful tic convulsif" to describe the association of HFS with ipsilateral trigeminal neuralgia in four patients. When Cook and Jannetta [49] reviewed the literature 64 years later, they found that 37 additional cases had been reported, and they added 11 of their own. In 15 of the patients collected from the literature, the posterior fossa had been explored. Eight patients had been found to have an ectatic basilar or vertebral artery ("cirroid aneurysm"); two, an arteriovenous malformation; and five, a tumor. Of Cook and Jannetta's 11 patients, 10 had compression of the trigeminal nerve at the pons by adjacent vessels and 11 had compression of the facial nerve at the brain stem by adjacent vessels (plus an ectatic vertebral artery in two instances and a meningioma in a third) [49]. Miyagi et al [215] treated one patient in whom both nerves were compressed by a tortuous vertebral-basilar artery complex. In three patients reported subsequently by Perkin and Illingworth [261], the trigeminal nerve was compressed by adjacent arteries in two and by a cholesteatoma in one; the facial nerve was compressed by an ectatic vertebral artery in one, by a posterior inferior cerebellar artery in one, and by a cholesteatoma in one. Other authors have made similar observations [4,78,89,211,260,333].

Yeh and Tew [364] have used the term *tic convulsif* in a different way; they mean the combination of HFS and geniculate neuralgia. They described two patients with this syndrome, both of whom were relieved by vascular decompression of the facial-acoustic nerve complex, including the nervus intermedius. Lamm [183], in 1963,

published the report of a similar patient who was relieved by decompression of the intratemporal portion of the facial nerve. And in 1969, Kempe and Smith [164] reported a patient with HFS and ipsilateral geniculate neuralgia thought to be due to a persistent primitive acoustic artery.

Jannetta [133,145] and Jannetta and Gendell [153] have contended that vascular compression of the medulla oblongata on the left side at the zone of exit of the vagus nerve is a cause of hypertension. Because of the close anatomical relationship of this area to the zone of exit of the left facial nerve, Jannetta has postulated that in some patients there is an association between left HFS and hypertension by the common mechanism of vascular compression. While operating upon 27 patients (all of whom had coexisting essential hypertension) for the treatment of a cranial nerve dysfunction syndrome due to vascular compression, such as trigeminal neuralgia, HFS, or glossopharyngeal neuralgia, Jannetta inspected the zone of attachment of the vagus nerve to the medulla. In 20 of the 22 patients whose operations were on the left side, he noted definite arterial compression of the medulla oblongata in the area between the glossopharyngeal and vagus nerves, and the inferior olive. However, he saw no such vascular compression in the five patients who had right-sided operations. Jannetta attempted left lateral medullary-vagal decompression in 14 of the 22 patients: 6 became normotensive without medication, 3 became normotensive with medication, and 2 had significant improvement of the hypertension.

Ehni and Woltman [71] studied the incidence of hypertension among their 106 patients with HFS and compared it with similar figures from 1000 control patients seen at the same institution. They concluded: "It is barely possible that hypertension is more common among patients with spasm who were less than 50 years of age than among other patients of the clinic of corresponding age (who probably have a higher incidence of hypertension than the population at large), but statistically the difference is not significant."

Among 30 personal patients, 8 of 19 (42%) with left HFS were hypertensive, as were 3 of 11 (27%) with right HFS. This difference is not statistically significant (X^2 test; $P = 0.70$). Attempted left lateral medullary-vagal decompression in three patients did not result in improvement of the hypertension.

Essential Blepharospasm

Essential blepharospasm is a syndrome of repetitive bilateral closure of the eyelids due to muscular contraction, especially of the orbicularis oculi [103,127,128, 195]. The muscles of the two sides contract simultaneously and symmetrically. Both eyes close involuntarily

ily, unpredictably, and repeatedly; seconds or even minutes may pass before they open again. Blepharospasm interferes significantly with vision when the blinking is frequent. It typically disappears during sleep. Like HFS, blepharospasm is a disorder of adults and has a female preponderance. For example, among the 264 patients reported by Grandas et al [103], the mean age of onset was 55.8 years and women outnumbered men by 1.8 to 1. In the series of 250 patients reported by Jankovic and Orman [128], 75% were women and in only 2.6% did onset occur before 40 years of age. According to Ludman [195] the EMG findings are no different from those of voluntary forced eye closure, showing asynchronous bursts every 30-100 msec.

Meige's Syndrome

Meige's syndrome is a primary or secondary movement disorder in which bilateral blepharospasm is accompanied by bilateral dystonic spasms of the lower facial or oromandibular muscles [338]. The spasms may even extend below the head, but this involvement is generally mild.

Spastic Paretic Facial Contracture

Spastic paretic facial contracture may occur alone or in combination with myokymia. Such a combination ordinarily implies a pathological abnormality in the brain stem such as a glioma, a tuberculoma, or multiple sclerosis [62].

Facial Myokymia

Facial myokymia is described by Cherington et al [46] as follows:

[A] continuous, undulating, spreading, involuntary movement limited to the facial muscles of one side. It almost always is associated with an intramedullary brainstem lesion. . . . The various brainstem lesions . . . that have been reported with facial myokymia are: pontine glioma, multiple sclerosis, metastatic tumor, acoustic Schwannoma, and pontine tuberculoma. . . . The electromyographic features of facial myokymia can help in establishing the diagnosis. There is considerable electrical activity in comparison to the modest clinical movements. The motor unit action potentials resemble normal motor units but occur spontaneously in rhythmic bursts at regular intervals. The frequency varies from 0.25 to 2.5 times per second. The units can occur in doublets, triplets, or multipliers. The clinical movement disorder is one of an undulating worm-like spreading movement which is rather subtle as compared with the more violent clonic movement seen with hemi-

facial spasm. . . . The EMG bursts in hemifacial spasm are very high frequency, asynchronous discharges as frequent as 250 per second.

Unfortunately (from the standpoint of clarity of classification), the term *myokymia* has also been applied to another type of facial movement with a much better prognosis, referred to as benign facial myokymia and sometimes thought of as minimal HFS [119,122]. Blair and Berry [27] have characterized this condition as follows:

Facial myokymia is a disorder of facial muscle movement characterized by fine flickering or quivering movements of individual facial muscle bundles. Usually the muscles around the eyelids are involved. The condition is usually unilateral. It occurs commonly in adults, with men and women being equally affected. The condition may be part of a more generalized benign or so-called essential myokymia involving other cranial and peripheral muscles. . . . In most cases no recognizable etiology can be determined. . . .

Habit Spasms

Habit spasms (idiopathic tics) are abrupt, jerky, repetitive bilateral or unilateral movements involving discrete muscle groups [187]. They mimic a normal coordinated movement, vary in intensity, and lack rhythmicity. According to Ehni and Woltman [71], this condition is distinguished

by the involvement of muscles other than those receiving innervation from the seventh cranial nerve, by its frequent onset in childhood, by its variability, by the substitution of one tic for another, by the ease with which the spasm may be reproduced voluntarily, by the fundamental compulsion that the patient feels to make the movement, by the essentially purposive character of the act and by the ability of the victim to control the movement for a short period.

Focal Cortical Seizures

Focal cortical seizures involving the contralateral facial muscles have clinical and electroencephalographic characteristics that are similar to those of focal cortical seizures involving the muscles of the contralateral limbs. In most cases the lower facial muscles are involved first, and the attack may be followed by some weakness of the affected muscles [346]. According to Wartenberg [346]:

The episodes in cortical epilepsy are shorter, more violent, and less frequent than those in hemifacial spasm. Fine, fascicular muscle twitchings, typical of spasm, do

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Postparalytic Hemifacial Spasm

Postparalytic HFS is probably the most difficult condition to differentiate from spontaneous HFS; it is the type of HFS that follows facial paresis such as that caused by Bell's palsy or trauma to the facial nerve. Postparalytic HFS has one or more of the following components that involve the muscles supplied by the affected facial nerve: contractures, spontaneous spasms, intrafacial associated movements (facial synkinesis), and weakness [346]. The intrafacial associated movements are involuntary movements of one or more of the facial muscles on voluntary or reflex contraction of another facial muscle; for example, an attempt to purse the lips or smile may also cause closure of the ipsilateral eyelids. HFS that occurs without a recognized antecedent injury to the facial nerve also exhibits one or more of these same components, but ordinarily the spontaneous spasms are the dominant feature. In contrast, contractures and intrafacial associated movements are usually the dominant features of postparalytic HFS.

In an electromyographic study of reinnervated muscle after facial nerve injury, Magun and Esslen [199] found that simple closure of the eyelids produced a simultaneous contraction of all facial muscles on the injured side. Although there was an identical repetition of this pattern of innervation each time the eyes were closed, the individual units discharged independently of one another. The units were limited to individual muscles and there was no evidence that giant units had formed.

Itagaki et al [123] reported in 1989 that electrophysiological examination is useful in differentiating spontaneous HFS from HFS following Bell's palsy. Specifically, they found differences between these two groups of patients by electromyography (maximum firing rate), electroneurography (ENoG value), and blink reflex testing (pattern of synkinetic potentials).

Various theories have been proposed to explain the development of facial synkinesis after facial nerve injury or Bell's palsy. These include aberrant nerve regeneration, ephaptic transmission between adjacent axons, and functional reorganization within the facial nucleus [199,207,234,346]. However, these points are still being investigated and discussed, and there is not general agreement on a single mechanism.

Tardive Dyskinesia

Lingual-facial-buccal dyskinesias are bilateral "uncontrolled and unintentional repetitive movements of

the tongue, lower face, and buccal and masticatory muscles. . . . The movements may be idiopathic or induced by neuroleptic treatment as a form of tardive dyskinesia" [56]. The idiopathic disorder tends to occur in elderly patients [56]. Tardive dyskinesia, persistent involuntary movements that follow the prolonged use of an antipsychotic drug, is encountered in patients with a wider age range although it does occur more commonly with increasing age [35,334].

Etiology and Pathogenesis

Since HFS was first recognized as a clinical entity more than a century ago, physicians have speculated about its etiology and pathogenesis, and about the anatomical location of the causative abnormality [71,156,367]. Over the years, it has become recognized that some patients (and animals [288]) with HFS have a lesion affecting the ipsilateral facial nerve at some point along its course, such as a megadolichovertebrobasilar anomaly (an ectatic, elongated, and tortuous vertebrobasilar arterial system; also called a cirroid, fusiform, racemose, or serpentine aneurysm) or a berry aneurysm [4,20,34,37-39,49,50,58,60,62,69,90,93,95,98,117,134,160,165,178,181,189,201,203,235,240,241,249,261,268,273,282,289,305,319,321,331,333,335,342,359], a neoplasm [5,16,49,53,55,57,59,62,70,78,89,93,117,134,152,185,188,191,197,210,211,216,217,256,257,260,261,283,284,303,317,323,324,344,350,353], an arteriovenous malformation [66,93,95,134,152,194,210,267,303,337], Pager's disease of the skull [30,31,36,47,93,94,116,254,324], or some other pathological lesion [5,14,21,42,51,95,164,170,171,181,182,250,251,262,298,302]. Despite this experience until recently a specific cause could not be identified in most patients with HFS. However, in the past two decades, evidence has accumulated that in most patients the condition seems to be due to compression, by an adjacent blood vessel (Figure 1), of the zone of exit of the facial nerve from the brain stem [9,12,13,16,17,19,26,28,40,44,49,72,75,79,86,88,90,93,95,102,105-108,110,111,124,125,131,132,134-152,154,157,163,168,169,173-176,192,193,201,218,220-232,236,238,248,252,263,266,274,275,279-281,286,291,292,294,296,300,304,347,351-354,357,359,360,365], a circumstance that may be contributed to by crowding within the posterior fossa caused by a primary or secondary reduction in posterior fossa volume [14,21,30,31,36,47,51,93,94,116,170,171,204,254,324,363] or by a focal mass such as a tumor within the ipsilateral or contralateral [99,251] posterior fossa.

In 1945, Ehni and Woltman [71] published an analysis of 106 cases from their own institution as well as a review of the pertinent medical literature to that time.

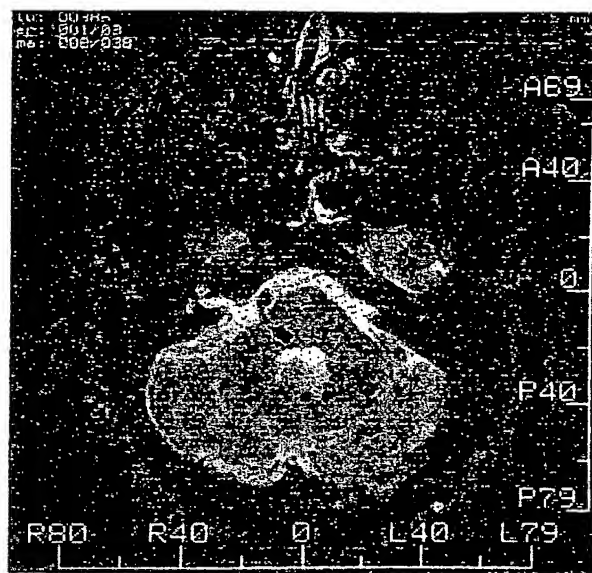


Figure 1. Magnetic resonance image of a 33-year-old man with a 6-month history of right hemifacial spasm. Arterial compression of the brain stem at the exit zone of the right facial nerve is shown (arrow).

Figure 2. Histological section showing the exit of the facial nerve from the brain stem. The lighter-stained central myelin extends as a truncated cone a short distance into the nerve (black arrows). The peripheral myelin is darker-stained. An adjacent vein is also shown (white arrow). (Modified from Digre and Corbett [62].)



They concluded that the basic abnormality in HFS is located somewhere along the pathway of the facial nerve between the facial nucleus and the stylomastoid foramen. Other authors have agreed, including those who have described or treated facial nerve compression in the cerebellopontine angle or within the temporal bone. Yet others have presented evidence that the location of the abnormality is within or central to the facial nucleus [32,71,346] or is distal to the stylomastoid foramen [59,256,324].

It has been the contention of Jannetta and co-workers [139,145,152] that in certain vascular compression syndromes of the cranial nerves, including HFS, the crucial point of compression is at the junction of the glial and nonglial portions of the affected nerve (Figure 2). The distance from the brain of this dome-shaped junction of the central glial axonal insulation and the peripheral axonal myelination by Schwann cells varies according to the specific nerve. Skinner [320] found in a series of human autopsy specimens that the average extension of glial spread into the facial nerve is 2.5 mm. This distance has been found to be slightly shorter in other studies [184].

Among Jannetta's 366 patients with HFS, the etiology was thought to be arterial in 323 (multiple arteries in 96), venous in 7, and both arterial and venous in 33; of the other three patients, one had a tumor, one had an

aneurysm [134]. Further with vascular this vascular facial nerve almost always [139,143], most common posterior experience

Among the offending veins. In 2 artery (PICA) anterior in The vertebral in four AICA was vertebral a case. This also encouraged [79] in which in 1, and the et al [16] in PICA in 14 reported by was AICA in the series PICA—18 Fukushima vertebral a

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aneurysm, and one had an arteriovenous malformation [134]. Furthermore, Jannetta noted that of the patients with vascular compression, those with typical HFS had this vascular effect on the antero-caudal aspect of the facial nerve exit zone, whereas those with atypical HFS almost always had the effect on the posterorostral aspect [139,143,144,148,149]. In Jannetta's series [139], the most common artery involved in typical HFS was the posterior inferior cerebellar artery. This was also the experience of Loeser and Chen [193].

Among 53 patients reported by Kondo et al [176], the offending vessels included 52 arteries and 2 petrosal veins. In 24 instances, the posterior inferior cerebellar artery (PICA) was involved, and in 24 instances, the anterior inferior cerebellar artery (AICA) was involved. The vertebral artery seemed to be the responsible vessel in four cases. In the series of Wilson et al [359], AICA was more often involved (12) than was the PICA-vertebral artery complex (9); a vein was implicated in 1 case. This general pattern of AICA predominance was also encountered in the series reported by Fairholm et al [79] in which AICA was implicated in 12 cases, PICA in 1, and the vertebral artery in 7; in the series of Auger et al [16] in which AICA was the relevant vessel in 20, PICA in 14, and the vertebral artery in 9; in the series reported by Baba et al [19] in which the distribution was AICA—54, PICA—38, and vertebral artery—11; in the series by Apfelbaum [13] with AICA—26, PICA—18, and vertebral artery—7; and in the series of Fukushima [88] with AICA—65%, PICA—16%, and vertebral artery—18%.

In a personal series of 74 patients, 1 had a meningioma in the ipsilateral cerebellopontine angle. Among the first 48, whose operative findings were analyzed [266], arterial contact with the facial nerve was noted in 46 (96%) patients, in 15 of whom there was visible anatomical distortion of the nerve. As in Jannetta's experience [139], it was not uncommon that more than one vessel seemed to contribute to the vascular compression in a single patient. In 22 instances the nerve was contacted by the PICA; in 17, by the AICA; and in 11, by the vertebral artery. In 10 other instances, an artery contacting the nerve could not be named because of insufficient exposure. One patient had osseous contact with the nerve, and one patient had no perceptible abnormality.

In contrast to these experiences, Adams and co-workers [78,162] could find a definite vascular abnormality in only 4 of 16 patients; in the other 12 there was no apparent abnormality. This has led to an ongoing debate between Adams [1,2] and Jannetta [140] about the etiology of HFS and the explanation of the favorable results of surgical treatment within the cerebellopontine angle.

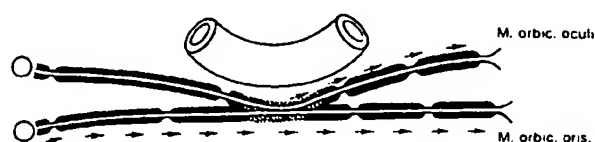
As evidence has accumulated about the pathological

conditions and anatomical location that seem to be important in the etiology of HFS, authors have also speculated about the specific pathophysiological mechanisms involved in its development [62]. Some have proposed that communication occurs between adjacent axons within the facial nerve, perhaps because focal compression and demyelination permit the formation of a false synapse (ephapse) [15,29,33,90,91,93-95,125,145,152,154,166,168,169,172,179,180,212,219,239,244-248,291,297,361]. Gardner [91] referred to the overall phenomenon of ephaptic transmission of a nerve impulse ("short circuiting") as "cross talk," and thought that this phenomenon could explain the pathophysiology of HFS (Figure 3). Based on various lines of evidence, Gardner [91] in 1966 concluded that although "the unsustained synkinesis which follows Bell's palsy can be explained by interaction between efferent fibers, the self-perpetuating synkinesis in hemifacial spasm is more compatible with a peripheral reverberating circuit set up between afferent (proprioceptive?) and efferent fibers at a point of compression."

Based on an extensive personal experience and a review of the literature, Nielsen [244] stated:

Many of the things we would expect to see if hemifacial spasm were mediated by ectopic/ephaptic excitation have in fact been demonstrated to occur in patients with this disorder: bidirectional cross-transmission between fibers; decreased conduction velocity in "pre-ephaptic" motor fibers; focal slowing of conduction over the suspected site of compression, suggested by an increased latency of the R-1 component of the blink reflex; lateral spread of orthodromic impulses leading to increased amplitude of the blink reflex and the occurrence of synkinetic responses in other facial muscles; auto-excitation, related to the passage of a single anti- or orthodromic impulse and with lateral spread of current often resulting in a "cascade effect" which causes clinically evident clonic-tonic spasms; and ectopic excitation induced by hyperventilation, presumably due to reduction in the concentration of extracellular calcium caused by respiratory alkalosis. All of these observations fulfill predictions made by the hypothesis that HFS is caused by abnormal conduction of impulses through the peripheral portion of the facial nerve, and the results of

Figure 3. Diagrammatic depiction of ephaptic transmission within the facial nerve at a point of vascular compression. (From Digre and Corbett, in *Advances in Neurology*, "Hemifacial spasm: Differential diagnosis, mechanism, and treatment," 1988.)



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our study provide evidence that ectopic excitation and ephaptic transmission are important in the pathophysiology of hemifacial spasm.

In addition [postoperatively], alterations in facial nerve function resolved over time in the sequence expected if the disorder was due to abnormal conduction in the peripheral facial nerve. The earliest sign that ephaptic transmission had been abolished was disappearance of isolated or synchronous afterdischarges, reflecting auto-excitation and "cross-talk" between single fibers. At the same time, the amplitude of the blink reflex became normal, followed by disappearance of synkinesis (the supraorbital reflex is probably conducted through the facial nerve as an asynchronous volley of impulses because of synaptic delays in the facial nucleus). Finally, there was marked decrease in the amplitude of the ephaptic response after supramaximal antidromic stimulation, indicating that lateral spread of current was activating fewer fibers. Disappearance of ephaptic transmission after supramaximal stimulation was considerably more delayed, but was eventually noted in almost all patients. The fact that in many patients an ephaptic response could only be elicited by an increased stimulus current indicates that at least it was necessary for a larger number of fibers to be depolarized postoperatively than preoperatively. Finally, by two to eight months postoperatively patients showed a significant decrease in the latency of the R-1 component of the blink reflex, which may be a direct indication that remyelination was taking place.

Because increased interstitial resistance in the paraxonal space can be regarded as a precondition for ectopic/ephaptic excitation, the early postoperative electrophysiological findings are critical in determining whether such excitation is really the pathophysiological mechanism causing HFS. During surgery the indentation in the facial nerve caused by a vessel overlying it often resolves when the vessel is lifted away. Conceivably, therefore, the primary effect of facial nerve decompression is to cause a decrease in interstitial resistance. This has predictable electrophysiological consequences. Lateral spread of current will be diminished and consequently ephaptic excitation of neighboring fibers will be abolished. The effects will be noted first for single fiber impulses or an asynchronous volley of impulses, because they generate minimal extra-axonal current flow. Later, ephaptic transmission triggered by the passage of a maximal synchronous volley of impulses, e.g., after a supramaximal stimulus, may also be abolished; but because the summated extra-axonal current flow generated by depolarization of a large number of fibers causes a major change in polarity in the interstitium between axons, this effect will not be seen as soon postoperatively as the first described.

A secondary effect of surgical decompression is to allow fibers to be remyelinated. However, because remyelination takes time and is probably incomplete when it does occur, the results of this process may only be noted electrophysiologically long after the surgical procedure.

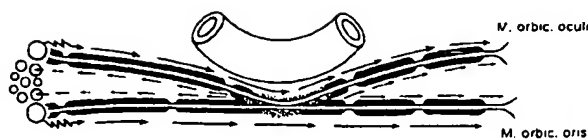
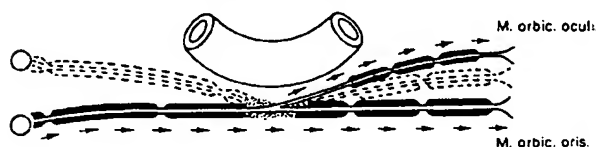


Figure 4. Kindling model. Diagrammatic depiction of excitation of the facial nucleus by vascular compression of the facial nerve. (From Digre and Corbett, in *Advances in Neurology*, "Hemifacial spasm: Differential diagnosis, mechanism, and treatment," 1988.)

A puzzling, but conspicuous phenomenon noted in patients recovering from HFS was the conversion from bidirectional to unidirectional ephaptic transmission, and the fact that transmission was always from the zygomatic towards the mandibular branch of the nerve. This uniform change in direction may in fact be explained by reviewing the natural history of HFS. The spasm typically is noted first in the inferior orbicularis oculi muscle, and progresses only over a period of years to involve lower facial muscles. Therefore, zygomatic branch nerve fibers may be more severely damaged (demyelinated) than mandibular branch nerve fibers. Consequently, the capacitance of zygomatic nerve fibers would be expected to be higher than that of mandibular nerve fibers, leading to greater resistance of zygomatic fibers to excitation. It is of interest that we have seen identical unidirectional ephaptic transmission in patients with HFS of short duration. Such findings are in keeping with those from studies of single fibers which showed that the direction of ephaptic transmission was always from more slowly to faster conducting fibers.

However, despite Nielsen's conclusions, other investigators, including some from his own institution, have postulated that the important pathophysiological changes in HFS occur within the facial nucleus, perhaps in response to a peripheral stimulus (Figure 4) [32,62,73,77,80,119,196,219-222,226-228,339,346]. Yet another hypothesis that has been proposed (but which has not found solid support in explaining the features of nontraumatic HFS) is that aberrant regeneration occurs within the facial nerve, perhaps from a point of nerve compression, such that some of the axons originally supplying one facial muscle become misdirected to another (Figure 5) [62]. Thus, the debate continues, and the pathophysiology of HFS remains under investigation at the present time.

Figure 5. Diagrammatic depiction of aberrant regeneration in the facial nerve occurring in response to vascular compression. (From Digre and Corbett, in *Advances in Neurology*, "Hemifacial spasm: Differential diagnosis, mechanism, and treatment," 1988.)



Treatment

In those few patients with an abnormality along the path of the facial nerve that can be detected radiologically, such as a neoplasm in the cerebellopontine angle, the treatment is directed against the lesion that has been demonstrated. This approach ordinarily will also relieve the HFS, especially if the surgeon ensures that no residual compressive effect on the facial nerve remains at the end of the procedure. However, most patients with HFS do not fall into this category and must be treated in other ways.

Various forms of nonoperative treatment have been tried for the relief of HFS, usually without much benefit. These approaches have included medicines of various sorts, psychotherapy, electrical stimulation, massage, and radiotherapy with the linear accelerator [3,10,71,73,81,104,112,177,179,186,196,211,299,339,346,362].

However, some patients have experienced improvement when taking haloperidol [25], clonazepam [115], carbamazepine [7,211,302,318], orphenadrine [120], or baclofen [299]. Alexander and Moses [7] stated in 1982 that there had been at least seven previous publications (dating back to 1964) concerning the use of carbamazepine to treat HFS; they found that among 46 reported cases, the incidence of complete control of symptoms was 22% and that of sustained improvement was 35%. In 1980, Hughes et al [120] reported the results of treatment of HFS with orphenadrine, an anticholinergic medication, for periods up to 18 months. Of the 13 patients so treated, 4 had no improvement and 2 had complete relief; the other 7 patients averaged 70% improvement. More recently, Sandyk and Gillman [299] reported the successful medical treatment of six patients with idiopathic HFS using baclofen, with follow-up intervals of 3 to 14 months.

In the early years of surgical therapy HFS was treated by totally or partially interrupting or injuring the peripheral trunk or branches of the facial nerve, which substituted some degree of facial weakness for abnormal movement [23,43,48,61,71,96,104,112,114,186,213,253,259,269,308,309,327,340,349]. Although the relief from the facial spasms was immediate, the injured or divided nerve ordinarily regenerated, with return of the HFS in 3 to 6 months or so [112].

Some surgeons, if they chose to treat by dividing the facial nerve trunk just after its exit from the stylomastoid foramen, then performed a nerve anastomosis using the hypoglossal or spinal accessory nerve to restore function and to prevent regrowth of the facial nerve into its distal channels [3,10,48,54,71,112,114,121,264]. However, cases have been reported in which the HFS returned despite a successful nerve anastomosis, apparently because of regeneration of the facial nerve along

old or new paths to the facial muscles [10,113,121,325].

An alternative to the operative exposure of the peripheral facial nerve trunk or branches was to injure one or more of these elements by the percutaneous injection of alcohol or phenol, or by the percutaneous insertion of a needle into the nerve [5,48,65,101,104,112,327,345]. Parenthetically, Harris and Wright [112] stated:

It is interesting to notice that in those cases in which clicking noises in the ear accompany the clonic facial spasms, these noises continue after the facial paralysis produced. This is because the nerve-supply to the stapedius muscle is on the proximal side of the alcohol injection, being given off within the middle ear. Yet within a day or two these clicking noises always disappear, probably owing to a reflex effect of the nerve paralysis upon the ganglionic nerve centres, inhibiting the efferent discharges from above.

Based on evidence that in some patients with HFS the facial nerve is abnormal within the facial canal, the goal of treatment has been the decompression of this segment of the facial nerve [8,166,167,183,189,190,211,214,270-272,339,358,361]. However, the enthusiasm for this approach has waned because of the high rate of recurrence of the HFS.

As indicated above, Gardner [93] postulated that HFS is the result of a reverberating circuit set up between afferent and efferent fibers at a point of facial nerve compression. He stated in 1968 [93]: "We have . . . learned that, when intracranial neurolysis fails, relief of hemifacial spasm may follow a second procedure in which the nervus intermedius is divided." In the same year, Crue et al [52] reported treating five patients with sectioning of the nervus intermedius intracranially with simultaneous gentle compression of the facial nerve. These approaches and the procedure of wrapping the facial nerve in the posterior fossa [78,162] may exert their beneficial effect solely by facial nerve trauma, a mechanism that has also been invoked by some authors to explain the relief afforded by microvascular decompression, a procedure to be discussed below [78].

Variations of the extracranial procedures discussed above, including those performed by a percutaneous approach, are still being done, primarily because they carry less risk than does intracranial surgery [64,73,81-83,97,118,124,200,212,214,293,295,296,306,310,332,336,339,341,366]. New approaches have been introduced as well, such as puncturing the facial nerve transtympanically [195,196,366], performing a longitudinal facial neurotomy within the third portion of the fallopian canal [45], inserting tantalum wire into the intratympanic segment of the facial nerve [205], or us-

ing a radiofrequency current to thermocoagulate fractionally the facial nerve percutaneously [22,118,158, 295]. Yet the basic problems remain—some degree of temporary facial paresis results, and the HFS returns with time.

In 1972, Wakasugi [345] published the results of treating a series of 239 patients by percutaneously inserting a needle into the facial nerve at the stylomastoid foramen. The induced facial palsy disappeared spontaneously within 1 or 2 months in the majority. The cessation of the HFS lasted from 2 to 27 months, with 47% of the patients relieved for more than 8 months.

Totoki et al [341] used Wakasugi's method to treat 225 patients. The facial paralysis produced recovered gradually (20% of 150 patients by 1 month, 77% by 2 months, 91% by 3 months, and 98% by 4 months). The HFS also returned, but over a longer period (12% of 120 patients by 6 months, 22% by 8 months, 50% by 10 months, 69% by 12 months, and 98% by 24 months).

Although Wakasugi stated that recurrent spasm could be controlled easily by a repeat procedure, Iwakuma et al [124] subsequently published a different view of this recommendation. They noted that 30 of their 110 patients had been treated previously by the needle insertion technique: "All 30 patients refused repeat nerve block because of severe pain during the procedure and excessive initial paralysis followed by early return of spasm."

In 1982, Elmqvist et al [73] reported the treatment of 20 patients with HFS by phenol blockade of the main trunk of the facial nerve. Immediately after the injection, a slight to moderate facial paresis occurred on the injected side, which usually subsided within 3 to 5 days. The spasms disappeared immediately after most injections, but they returned in most patients after 6 to 12 months.

Hori et al [118] used a fluoroscopy-assisted technique of percutaneous radiofrequency facial nerve coagulation at or near the stylomastoid foramen in 27 patients. Partial facial weakness resulted in 60% of the cases, but invariably disappeared within 1 to 4 months. At the time of publication, only three patients had noted recurrence of spasm. However, the average duration of follow-up was not specified.

Iwakuma et al [124] treated 21 patients by partial sectioning of the facial nerve trunk just distal to the stylomastoid foramen. Hemifacial spasm recurred within 1 year in 10 patients (47%), and only 3 patients, followed for 18 months to 5 years, achieved relief of spasm.

Fisch and co-workers [64,81,82] have favored the technique of selective neurectomy for the treatment of HFS. This procedure involves the resection of extra-temporal facial nerve branches involved in the hyperki-

netic facial movements with preservation of sufficient innervation to avoid the appearance of facial paralysis. In 1986, Dobie and Fisch [64] and Fisch [82] reported that 94 patients with HFS had been treated in this way. Results were given for 39 patients who had been followed for 1–12 years: 10 had 100% relief, 10 had 75% relief, 11 had 50% relief, 1 had 25% relief, and 7 had 0% relief. The spasm was relieved 50% or more in 13 of 16 patients followed 1–3 years, 6 of 8 followed 4–6 years, and 12 of 15 followed 7–12 years.

Iwakuma et al [124] had less favorable results from the selective neurectomy of facial nerve branches. The HFS recurred within 1 year in 12 of 20 patients and only 3 patients followed for 2 to 3 years had relief of spasm for that length of time.

In recent years, type A botulinum exotoxin has been injected in small doses into various facial muscles to reduce their contractions; this has been used especially to treat blepharospasm and HFS [67,74,177,301,324, 343]. Complete or almost complete relief of symptoms is achieved in 90% to 100% of patients with HFS. However, relief is temporary in almost all cases, lasting on average 3 to 4 months [177]. Therefore, injections have to be repeated periodically for an indefinite time.

Because of dissatisfaction with the results of the various treatments discussed above, there has been increasing interest in a nondestructive approach aimed at removing the presumed compression of the facial nerve without injuring the nerve. This procedure, the decompression of the facial nerve within the posterior cranial fossa, had its beginnings before 1960, but has been performed mainly since 1970 [92,142,154,276–278].

Microvascular Decompression of the Facial Nerve

Background

In 1960, Gardner [92] reported a patient who had been substantially relieved of HFS for 5 years following the gentle manipulation of the facial nerve with a nerve hook introduced into the porus acusticus. During that operation, after the nerve manipulation, a piece of Gelfoam (absorbable gelatin sponge; The Upjohn Company, Kalamazoo, MI) was placed beneath the internal auditory artery to separate it from the eighth nerve (the patient also had vestibulocochlear dysfunction).

By 1962, Gardner had treated 19 patients with HFS by neurolysis of the facial nerve in the cerebellopontine angle; in 7 of these, the nerve was found to be compressed by a redundant loop of the anterior inferior cerebellar or internal auditory artery [95]. In 18 of the 19 operations, the facial nerve was gently manipulated with a nerve hook, and in several instances the nerve also was irrigated by a forceful stream of Ringer's solution. Gardner and Sava [95] stated:

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[In the seven cases] in which the nerve was compressed and distorted by a loop of a normal artery, the causal relationship may be questioned in view of Sunderland's . . . finding that a large loop of the anterior inferior cerebellar artery was related intimately to the 7th and 8th nerves in 64 per cent of routine autopsies. . . . Despite the incidence of such vessels, it is difficult to argue with the fact that, in these 7 cases of hemifacial spasm, freeing of the nerve from the vessel and the interposition of a bit of Gelfoam where feasible, was followed by relief in every case and at the cost of mild and transient weakness in only 1 instance. It must be noted however that in the last 3 cases, in addition to this manipulation, a bundle of fibers, believed to be nervus intermedius, was divided.

Based on an experience with the surgical treatment of trigeminal neuralgia (achieved in collaboration with Rand) [130,155], Jannetta postulated that the crucial point of vascular compression as the cause of HFS is at the zone of exit of the facial nerve from the brain stem, where the central myelin changes to peripheral myelin. His first operation to decompress the facial nerve was in February 1966. In 1970, Jannetta [142] reported:

In the first patient . . . the 7th and 8th cranial nerves looked normal until the brain stem was approached; at this point a small vein along the surface of the pons above the facial nerve was found compressing and distorting this nerve. . . . The vein was coagulated and divided. . . . In the second patient . . . a tortuous left vertebral artery was found compressing the facial nerve at the point just adjacent to the brain stem. This was mobilized and held away from the brain stem by placing gelfoam between the vessel and the brain stem away from the facial and auditory nerves. . . . Five more patients have been operated upon, all with classical hemifacial spasm. All had vascular compression-distortion of the facial nerve at the brain stem. Three patients in whom the facial nerve was not traumatized awoke with hemifacial spasm which gradually disappeared postoperatively. They have remained free of spasms and without facial weakness.

As Gardner and Sava [95] noted, normally within the posterior cranial fossa there are close anatomical relationships between various cranial nerves and blood vessels [68,159,184,206,208,209,242,243,285,287,326,328-330,348]. In particular, the AICA, internal auditory artery, vertebral artery, and PICA lie close to the facial nerve.

For example, Watt and McKillop [348] wrote about their postmortem specimens:

The main trunk of the anterior inferior cerebellar artery shows many and varied relations to the roots of the

facial, intermediate and acoustic nerves. It lies either dorsal to or ventral to the nerve roots; it may loop around them or may pass between any two of them. In the vast majority of cases the internal auditory artery arises from the anterior inferior cerebellar artery and not from the basilar artery, as is stated in the textbooks. The internal auditory artery may occupy many positions as it emerges with the nerves. It may be either dorsal or ventral to them, between any two of them, medial to the facial nerve or lateral to the acoustic nerve.

Sunderland [330] commented that the PICA "frequently loops upwards ventral to the facial and auditory nerves at their site of origin, where it may compress them backwards against the pons or the middle cerebellar peduncle." He also noted that a tortuous vertebral or basilar artery may compress the brain stem at the site of origin of these nerves; such compression by a vertebral artery was found on 7 occasions on the right and on 20 occasions on the left among 210 specimens [330].

In 1980, Martin et al [206] published the results of a very detailed analysis of the relationships of the AICA and the facial-vestibulocochlear nerve complex in 50 cerebellopontine angles from 25 adult cadavers. In each instance one or more arterial trunks were found to course in close proximity to the nerves. The premeatal segment of such arteries was usually anteroinferior to the nerves, whereas the postmeatal segment was most commonly posteroinferior, superior, or posterior to or between the nerves.

Matsushima et al [208] examined the cisternal portion of the facial nerve and its contact arteries in 35 sides of 20 brains from autopsied adults who had not had HFS. One point of arterial contact was found on 10 facial nerves, two points on 20 nerves, and three points on 4 nerves. Such points of contact were noted at the nerve root exit zone of 24 of the 35 facial nerves (69%), with two points of contact in 5 nerves. The contact arteries at the nerve root exit zone included 24 AICAs, 3 vertebral arteries, and 2 PICAs.

These various studies have emphasized the close relationships that exist normally between the facial nerve and the adjacent vessels in the cerebellopontine angle. They also raise the possibility that the surgeon who moves an artery or divides a vein to decompress the facial nerve at the pontomedullary junction is achieving a beneficial result by mild injury to the facial nerve (all are achieving a result by injury) by the physical manipulations of the dissection, by the pressure from the material that is left behind to maintain the separation between a vessel and the nerve, by the heat generated by the bipolar cautery, by ischemia from vascular compromise, or by some other mechanism [1,2,11,17,24,78,138,140,162,198,204,237]. However, no matter what the actual reason, this approach to treatment has proved

effective. Many authors have reported their experience with microvascular decompression of the facial nerve for the treatment of HFS [12,13,16,17,19,26,28,44,49,72,75,79,88,102,110,111,124,125,131,134-137,139,141-152,157,163,168,169,173,176,192,193,236,238,263,266,281,286,292,294,296,300,351,353,359,360,365].

Technique

This procedure is usually performed with the patient in a lateral recumbent or sitting position [12,13,88,136,137,139,144,148,151,152,176,352]. After the ordinary preoperative preparations have been made, as for any craniotomy or craniectomy [356], and general anesthesia has been induced, the patient is positioned on the operating table with the head immobilized in a pin head holder.

If the operation is to be performed in the sitting or lounging position, an intra-atrial catheter is inserted while the patient is still supine, and after the upright position has been achieved, a Doppler monitor is placed on the anterior chest wall over the heart so that venous air embolism may be detected if it occurs during the operation. The upper and lower limbs are padded, positioned, and immobilized so that they are simultaneously supported and protected from inadvertent injury. Before the head holder is locked, the patient's head is flexed forward and the face is rotated 10° to 15° toward the side of the operation.

If the operation is to be performed in the lateral recumbent position, a route of lumbar cerebrospinal fluid (CSF) drainage (via one or two lumbar puncture needles or a subarachnoid catheter) is usually established before fixation of the head to aid in exposure of the zone of exit of the facial nerve from the brain stem. After this has been accomplished a soft chest roll is placed beneath the contralateral (lower) axilla and the dependent arm is supported to avoid compression, traction, and venous stasis. The lower limbs are padded and immobilized. The patient's head is flexed forward and away from the side of the operation. The head holder is locked, and the ipsilateral (upper) shoulder is drawn gently into a caudal and anterior position with tape to provide the surgeon better access to the retromastoid region. The entire operating table is then rotated in a head-up direction to bring the surgical field into a horizontal position.

Intraoperative auditory evoked potential monitoring has been shown to be valuable in reducing the incidence of ipsilateral deafness as a consequence of microvascular decompression of cranial nerves in the posterior fossa. This will be discussed in more detail below in the consideration of operative complications. If such monitor-

ing is to be used, the final electrode attachments are made before draping.

An area behind the ear is shaved, prepared with antiseptic solutions, and draped as a sterile field. A linear scalp incision is made along the mastoid crease, beginning at or slightly below the level of the top of the pinna. The linear incision is then carried down to the bone, which ordinarily requires coagulation and division of the occipital artery and division of the lesser occipital nerve. The periosteum and overlying soft tissues are stripped off the underlying bone, including the upper posterior face of the mastoid process. A small retromastoid craniectomy or craniotomy is created, positioned so as to expose the posteromedial aspect of the sigmoid sinus in the lateral portion of the cranial opening. The inferior margin of the cranial opening should be low so that the remaining bone is extending directly away from the surgeon and no lip is left to obscure the surgeon's view along the cranial base. If a craniectomy is performed, it is safest to make the initial perforation in the superomedial aspect of the proposed cranial opening and to then gradually extend the opening laterally and inferiorly with a rongeur or drill, taking care not to open the sigmoid sinus.

Frequently, mastoid air cells will be opened during the craniectomy or craniotomy. These should be waxed shut to keep fluid such as irrigation fluid, CSF, or blood from collecting within the middle ear. Waxing of the mastoid air cells also prevents any CSF that might leak through the dural incision postoperatively from exiting through the middle ear and eustachian tube, thus putting the patient at risk for meningitis.

After the cranial opening has been made and the bone edges waxed, the dura mater is opened inferiorly and laterally with a curved incision. An adequate inferior and lateral cuff is left to permit the later closure of the dura; this is retracted temporarily to provide exposure. Exposure is further facilitated by the intravenous administration, early in the operation, of mannitol and/or furosemide. Just before the dura mater is opened, CSF is drained from the lumbar subarachnoid space (if the patient is in the lateral recumbent position). After the dural opening, CSF is evacuated from the inferior and superior cerebellopontine cisterns.

During the intracranial portion of the operation a microsuction tip is used and the suction is reduced to 80 torr or less, which reduces the possibility of suction injury of the nerves and vessels in the cerebellopontine angle. With the help of the operative microscope and the use of microtechnique, dissection is carried anteriorly across the skull base, within the subarachnoid space and beneath the cerebellar hemisphere, until the ninth, tenth, and eleventh cranial nerves are visualized. The surgeon then dissects across the superior aspect of the

glossopharyngeal nerve, the first branch of the facial nerve, and the foramen of the facial nerve. Throughout the operation, the patient is used to enter the foramen in a careful manner, such as a compression.

The nerve at its exit from the surgeon's best way to an artery can be seen at the nerve at the places the material such as Unipoint I. Teflon felt (MA) to maintain a fashioned a arterial pulse effect on the a vein appears displaced if small.

As an alternative, an offending can be held or more slowly [88,281]. In it is encouraged of the level injury stretching, r

After the the dural incision. This order suture without suboccipital least a portion to replace the desires. If the probably not late cranioplasty risk of infection bony defect. The muscles, reapproximated.

glossopharyngeal nerve medially to expose the exit zone of the facial nerve. To complete the exposure, the surgeon ordinarily must retract the flocculus of the cerebellum and the choroid plexus, which protrudes through the foramen of Luschka. The anteromedially positioned facial nerve is usually gray, whereas the more posterolateral auditory nerve is yellowish-white in color. Throughout the dissection, a self-retaining retractor is used to enhance the exposure by retracting the cerebellum in a cephalad direction, but the surgeon must be careful to avoid potential detrimental effects of retraction such as injury to the auditory nerve from direct compression, stretching, or ischemia.

The nature of the vascular compression of the facial nerve at its exit zone will vary, and it is important that the surgeon inspect this area well before deciding on the best way to relieve the compression. Most commonly, an artery such as AICA, PICA, or the vertebral artery can be seen to be lying against or distorting the facial nerve at the brain stem, in which case the surgeon displaces the vessel away from the nerve and inserts some material such as Ivalon sponge (polyvinyl alcohol foam; Unipoint Laboratories, Highpoint, NC) or shredded Teflon felt (USCI Division of CR Bard, Inc., Billerick, MA) to maintain the separation. This material should be fashioned and placed in such a way as to dissipate the arterial pulsations without producing a significant mass effect on the nerve. In the unusual circumstance where a vein appears to be the offending vessel, it can be displaced if it is large, or coagulated and divided if it is small.

As an alternative to the insertion of material between an offending vessel and the facial nerve, such a vessel can be held away from the nerve by the insertion of one or more slings that are sewn to the adjacent dura [88,281]. In the rare circumstance where no abnormality is encountered, the surgeon may proceed to the closure of the operative defect, or may first induce a low-level injury of the facial nerve by mildly compressing, stretching, rubbing, or wrapping the nerve.

After the self-retaining retractor has been removed, the dural incision is sutured closed in water-tight fashion. This ordinarily can be accomplished with a running suture without the need for a dural graft. Because the suboccipital muscles will be reapproximated over at least a portion of the cranial opening, it is not necessary to replace the bone, but this can be done if the surgeon desires. If the mastoid air cells have been opened it is probably not a good idea to perform a methyl methacrylate cranioplasty as part of the closure because of the risk of infection. When the bone is not reinserted, the bony defect may be filled by the insertion of Gelfoam. The muscles, fascia, subcutaneous tissue, and skin are reapproximated with sutures in anatomical layers, and a

sterile dressing is applied. The patient is allowed to awaken after the lumbar puncture needles or drain and the evoked potential leads have been removed.

After overnight observation in an intensive care unit, the patient ordinarily can be moved to a medium care room. Although many patients notice immediate relief, in some the HFS persists for days or weeks before it subsides, presumably the period required to permit recovery within the previously compressed portion of the facial nerve.

Results

Jannetta, who pioneered the operation of microvascular decompression for the treatment of HFS [49,72,105-108,131,132,134-152,154,157,218,220-232,248,291], reported in 1980 [145] and subsequently [139,143,144,148,149] his results with 229 patients. Of these, 201 (87.7%) had no spasm after one operation, 12 (5.2%) had no spasm after a second procedure, 11 (4.8%) were partially symptomatic, and 5 (2.2%) were not helped. Subsequently, Jannetta [134] reported the outcome of 366 patients. Initially, 215 (58%) had a complete response, 141 (39%) had a partial response, and 10 (3%) had no response. The long-term results among 334 patients followed for 12 to 189 months (mean, 68 months), with a 10% reoperation rate, showed that 298 (89%) had a complete response, 17 (5%) had a partial response, and 19 (6%) had no response.

In 1980, Kondo et al [176] reported the outcome of microvascular decompression of the facial nerve in 44 patients with HFS who had been followed for more than 1 year postoperatively. They used the classification system of Jannetta et al [152] to assess their results, but reduced any assessment by one grade if the patient had a postoperative hearing deficit that lasted more than 1 year. Among their 44 patients, the outcome was excellent in 24, good in 12, fair in 7, and poor in 1. The authors encountered no recurrence of HFS in their patients during the follow-up period. They also found that among 10 patients with preoperative facial weakness (that had not been induced by a destructive operation), 8 noted recovery postoperatively.

Iwakuma et al [124] published in 1982 the results of microvascular decompression in a series of 74 patients with HFS. Of these, 72 (97%) had complete relief, 1 had marked improvement, and 1 had no improvement. During a follow-up period of 1 month to 3 years, only one patient experienced a recurrence.

In contrast, of 20 patients reported by Loeser and Chen [193], 3 failed to benefit from the operation and awoke with their spasm unchanged. In addition, 5 of the

initially cured patients suffered recurrences 10 to 17 months postoperatively.

In addition to reporting their own 20 patients in 1983, Loeser and Chen [193] surveyed the results of 15 other series of patients who were treated for HFS by microvascular decompression. The 433 patients from the 16 series had 450 operations: 366 (84%) were "cured" initially and 17 (4%) were "cured" by a second operation. The incidence of relapse after complete cessation of spasm was less than 10%. However, the length of follow-up in the 16 series was as short as 1 month.

In 1986, Auger et al [16] evaluated the results of microvascular decompression in 54 patients, 51 of whom had been followed postoperatively for 3 months to 10 years (average, 3.9 years). The condition was relieved completely in 44 (81%) patients after a single procedure, but 6 had recurrence from 3 months to 2 years postoperatively. Five (9%) patients had improvement from the initial operation and five (9%) had no benefit.

We reported in 1984 the results of microvascular decompression for the first 48 of a personal series of 74 patients with HFS [266]. After an average follow-up period of 42.5 months, 30 (62.5%) had complete relief (excellent result) and 12 (25%) had only infrequent and mild periorbital twitching (good result). Six patients either noted no significant improvement or sustained a recurrence after initial relief. A later assessment of 41 of these patients who were followed from 5 to 12 years (average, 8.1 years) postoperatively showed that initially 32 had an excellent result and 6 had a good result. This favorable immediate outcome tended to persist with time. Of the 32 with an excellent result, only 3 experienced recurrence, at 1, 6, and 54 months after operation, respectively. Three of the 41 patients underwent a second operation. At the time of last follow-up, 30 had an excellent result, 6 had a good result, and 5 had significant residual or recurrent HFS.

Among the entire group of 74 patients, 7 have had a reexploration. In contrast with Jannetta's experience [139], in no case had the previously inserted sponge slipped out of position and in most there was no obvious explanation for the continuation or return of the HFS such as persistent or recurrent vascular compression.

Complications

From the nature of microvascular decompression for HFS one would expect that the complications would center around inadvertent injury to the cranial nerves and vessels in the lower cerebellopontine angle, and this is the case [16,79,193,231,236,292,307,359]. But other problems have also been reported, some of which are related to the sitting position. In their 1983 review of 16 reported series totaling 433 patients with HFS,

Loeser and Chen [193] summarized the complications of 450 microvascular decompression operations. There were 341 (76%) operations with no complications, 38 (8%) with temporary complications, and 71 (16%) with permanent complications. Among the complications were 58 (13%) instances of auditory nerve dysfunction and 26 (6%) instances of facial nerve dysfunction. There was one (0.2%) reported death.

In the series of 74 patients reported by Iwakuma et al [124], a postoperative reduction in auditory acuity was noted in 12 (16%). Among the 53 patients of Kondo et al [176], 18 awoke with ipsilateral reduction of hearing: 9 improved within 3 months, but 9 (17%) sustained a permanent loss. A substantial ipsilateral hearing loss or permanent deafness was noted in 8 (15%) of 54 patients reported by Auger et al [16]. Mori et al [236] reported a significant postoperative hearing disturbance in 12 (18%) of 65 patients, and Saito [294] noted a permanent hearing loss greater than 10 dB in 6 (26%) of 23 patients.

In a series of experiments in dogs and monkeys, Sekiya and co-workers [311-316] tried to elucidate the pathophysiological mechanisms involved in the production of hearing deficits during cerebellopontine angle surgery. The operative manipulations performed in these experiments were the same as those used in analogous human surgery.

[In the dogs] as a result of the operative manipulations, petechial or confluent hemorrhages occurred at the compressed portions of the cochlear nerve, and intravascular clots were often observed. Disintegration of the nerve fibers was verified by ultrastructural examination. Moreover, rupture of the microvasculature within the cochlear nerve occurred at locations remote from the operative site, due to stretching of the nerve trunk. The Obersteiner-Redlich zone, the Schwann-glia junction of the cochlear nerve, was a locus minoris resistentiae in CP angle surgery; the vasa nervorum easily bled at this zone and the peripheral and central myelins easily separated at their junctional zones. . . . [316]

In rhesus monkeys, in contrast, the most common histological findings were avulsions of the internal auditory artery and cochlear nerve fibers at the fundus of the internal auditory canal (area cribrosa) [313,315]. These phenomena were thought to explain the abrupt loss of auditory evoked potentials that occurred in 4 of the 16 monkeys during retraction of the cerebellum or cochlear nerve.

In a personal series of 74 patients, the complication rate tended to diminish as the experience of the surgeon grew, with the exception of the incidence of significant ipsilateral hearing loss, which did not improve until the institution of intraoperative monitoring of auditory evoked potentials. The complications encountered

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among the first 48 patients included one instance of encephalopathy from arterial air embolism, two of anosmia, two of significant ipsilateral hearing loss, one of significant dysequilibrium, and two of glossopharyngeal/vagal dysfunction [266]. The minor complications included aseptic meningitis (3), phlebitis (1), drug reaction (1), slight facial weakness (2), mild reduction in hearing (1), and mild dysequilibrium (1). In addition, it was common to note a temporary ipsilateral conductive hearing loss because of fluid within the middle ear.

Prior to the institution of intraoperative auditory evoked potential monitoring at our hospital in 1984, 10 (6.6%) of 152 primary microvascular decompression operations for HFS or tic douloureux were followed by a profound ipsilateral hearing loss or deafness. Subsequently, however, none of 109 primary operations (assessed through June 1989) caused profound hearing loss or deafness [275,357]. This has also been the experience of Jannetta and co-workers, [107,145,148] who noted profound ipsilateral hearing loss or deafness in 16 (7%) of 229 patients following microvascular decompression for HFS during a period (1971-1979) before they began to monitor auditory evoked potentials in the operating room. During a subsequent period, with such monitoring, this same group noted only two (1.4%) instances of significant hearing loss after 140 microvascular decompression operations [230]. It is of interest that one of these two patients was being operated upon a second time for HFS. Recently, we have had two patients who lost hearing during a second microvascular decompression operation for recurrent HFS despite intraoperative monitoring of auditory evoked potentials, which represents two (29%) of seven patients having such surgery between 1977 and 1990. In both cases, wave V of the evoked potential was lost abruptly during dissection around the previously placed Ivalon sponge. This maneuver seems especially hazardous in regard to auditory morbidity.

Among the other surgical complications experienced by Jannetta's 229 patients were nine instances of immediate postoperative facial weakness, six of which persisted, and seven instances of delayed postoperative facial weakness, one of which persisted. There was also one patient who noted facial hypalgesia postoperatively. Serous otitis media was noted in 18 patients, aseptic meningitis in 13, bacterial meningitis in 1, wound infection in 1, CSF rhinorrhea in 8, tension pneumocephalus in 1, pneumonia in 4, pulmonary embolism in 1, and upper gastrointestinal bleeding in 2 [139,148].

Hanakita and Kondo [110] have noted that serious complications can follow microvascular decompression operations, even when they are performed by neurosurgeons who have considerable experience with this technique. Among 239 patients with hemifacial spasm whom they treated in this way, nine had serious compli-

cations, as follows: intracerebellar hematoma with acute hydrocephalus, cerebellar swelling with acute hydrocephalus, brain stem infarction, traumatic aneurysm, supratentorial acute subdural hematoma, cerebral infarction, intracerebral hemorrhage, and status epilepticus (two cases). Two of the nine patients died and three were left with a neurological deficit.

Wilson et al [359] also reported a death following microvascular decompression in a series of 22 patients with HFS. This was due to a cerebellar hematoma caused by an acute hypertensive crisis immediately after the operation. Rushworth and Smith [292] noted two instances of brain stem infarction among nine patients undergoing microvascular decompression for HFS.

Jannetta [132] has pointed out that several factors can cause hypertension in the setting of microvascular decompression. These include the application of a pin head holder, manipulation of the trigeminal nerve, excessive retraction of the cerebellum and brain stem, interruption of key veins with resultant venous congestion, and disturbance of arterial perfusion of the hindbrain. With or without hypertension, such events can result in hemorrhage or infarction within the brain. Jannetta also stated that the occasional occurrence of supratentorial intracerebral hemorrhage at his institution [109] had ceased after changing the operative approach from the sitting to the lateral decubitus position [132].

In the sitting position, the brain sags with the release of CSF; this can lead to subdural hematoma formation, especially in an elderly patient. In addition, cerebral blood flow may diminish, with reduced cerebral perfusion. Commonly, air enters the subarachnoid spaces and/or ventricular system, producing headache and nausea in the initial postoperative period. However, the most dangerous aspect of the sitting position is the potential for significant venous air embolism. In a personal series of 152 posterior fossa microvascular decompression operations (133 of which were performed with the patient sitting), venous air embolism, as suggested by changes in the sounds of the precordial Doppler monitor, was confirmed in 56 by aspiration of air from the intra-atrial catheter or by a sudden fall in the end-tidal P_{CO_2} [266]. It resulted in brief hypotension in only three patients, but one patient suffered a significant arterial air embolus, presumably through an occult patent foramen ovale.

Prevention of Complications

With any operative procedure, the acquisition of experience by the surgeon and surgical team will ordinarily produce better results, with improved outcome and fewer complications [132,357]. In addition, however, the use of specific techniques can further reduce the

occurrence of adverse phenomena resulting from microvascular decompression for HFS.

As mentioned in the previous section, most of the complications of that operation involve inadvertent injury to the cranial nerves or vessels in the lower cerebellopontine angle or are related to the use of the sitting position. Of these, the most common are dysfunction of the auditory and facial nerves.

We and others now routinely monitor brain stem auditory evoked potentials (BAEPs) during posterior fossa operations for microvascular decompression of cranial nerves [9,84,86,105-108,218,223,230,231,252,265,274,275,279,280,304,347,357]. In 1982, Raudzens and Shetter [280] concluded:

Intraoperative BAEP's can be reliably and routinely recorded in an operating room environment. They provide a good predictor of postoperative auditory status, and may have prevented permanent neurological deficits in a small segment of patients by alerting the surgeon to potentially reversible abnormalities.

Also in 1982, Grundy et al [106] reported that retraction of the eighth nerve, cerebellum, or brain stem was associated with BAEP deterioration during 22 of 54 operations in the cerebellopontine angle: "Typically, Peak V latency increased continually after retractors were placed. . . . The BAEP changes related to retraction invariably returned toward normal after repositioning or removal of retractors, and hearing was preserved in each case."

In our own experience, 10 (6.6%) of 152 microvascular decompression operations performed without BAEP monitoring were followed by a profound ipsilateral hearing loss [357]. During the 109 subsequent operations performed with such monitoring, the intraoperative BAEP changes were as follows: in 68 there was less than a 1 msec change in wave V latency, in 26 there was more than a 1 msec change, in 12 there was a transient loss of wave V, and in 3 there was a persistent loss. The postoperative hearing losses were all mild, occurring in 3 of the 68 operations with less than a 1 msec change, in 2 of the 26 with more than a 1 msec change, in 3 of the 12 with a transient wave loss, and in 1 of the 3 with a persistent wave loss. No monitored patient had a profound hearing loss, which represents a statistically significant difference when compared with the nonmonitored patients (Table 2).

However, evoked potential monitoring is not an absolute safeguard against deafness. Even with direct intraoperative monitoring of auditory compound action potentials from the eighth nerve [223,224,229], Møller and Møller [231] noted that 1 of 39 patients undergoing a first microvascular decompression operation for HFS

Table 2. Audiological Morbidity After Microvascular Decompression

BAEP monitoring	Number of operations	Auditory outcome		
		No deficit	Mild deficit	Profound deficit
No	152	134 (88.2%)	8 (5.3%)	10 (6.6%)*
Yes	109	100 (91.7%)	9 (8.3%)	0*

Source: Wilkins et al [357].

Abbreviation: BAEP, brain stem auditory evoked potentials.

* These findings differ significantly from random variation by Chi-squared statistic with Yates correction ($\chi^2 = 8.136$, $P = 0.017$).

"lost his hearing instantaneously during decompression of the facial nerve." Likewise, Nishihara et al [252] encountered a severe reduction in hearing in 2 of 94 patients having microvascular decompression as treatment of HFS or tic douloureux, despite both BAEP and direct auditory compound action potential monitoring. Furthermore, as mentioned above, the dissection involved in reexploration of the cerebellopontine angle in a patient with persistent or recurrent HFS is especially hazardous. Two (29%) of seven such patients in the author's practice sustained ipsilateral deafness despite intraoperative BAEP monitoring; in both cases, the evoked potentials were lost abruptly and did not recover despite immediate cessation of retraction and operative manipulation.

In 1987, Møller and Jannetta [225] reported their experience with the intraoperative monitoring of facial electromyography responses in 67 patients with HFS. The thrust of their study was not the prevention of facial nerve injury during microvascular decompression, but rather was concerned with the identification of the adequacy of the decompression. These authors found that electrical stimulation of the zygomatic or temporal branch of the facial nerve produced a response recorded from the mentalis muscle (lateral spread) in all of the patients at the start of the operation, and that this lateral spread of antidromic activity disappeared (44 cases), was diminished (16 cases), or remained unchanged (7 cases) as a result of the procedure. More importantly, they noted that the degree of reduction of the response correlated with the effectiveness of the procedure in abolishing the HFS. Møller and Jannetta [225] concluded:

[If] cure of hemifacial spasm is defined as absence of spasm, the overall cure rate in this series of 67 patients was 84%. If all operations had been continued until the lateral spread response was eliminated, it could have been expected that not more than two patients would have had spasm after the operation, thus boosting the cure rate of this procedure to 97%. . . . In cases in which there are several blood vessels in contact with the

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facial nerve, this technique greatly assists in identifying which vessel is causing the spasm, and has reduced the number of patients who have had to undergo reexploration because of persistent spasm after the operation.

The chief risk of using the sitting position for microvascular decompression is venous air embolism. Apfelbaum [13] and others believe that it is necessary to have the patient paralyzed and on controlled ventilation, not only to reduce motion in the field but, more importantly, to prevent the patient from developing a gasp reflex should a small amount of air embolization occur, which could then result in a rapid and massive air embolism. As an important precautionary measure, a Doppler monitor is placed over the precordium and is tested by the sudden injection of fluid through the intra-atrial venous catheter after the patient is sitting but before the skin incision is made. This monitor is very sensitive and will ordinarily detect small amounts of intravenous air (as little as 0.12 to 0.25 mL in a dog model) [202]. Such air embolism is common during posterior fossa microvascular decompression operations, but if proper techniques are used for its detection, it can ordinarily be managed by removing air through the intraatrial catheter, raising the venous pressure, and flooding the operative field with fluid until the venous portal of entry can be found and sealed [6,202]. If these maneuvers prove insufficient, the patient's head can be lowered until the venous opening is closed.

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Please supply the following:

TI FACIAL NERVE PAIN EXCLUDING TIC DOULOUREUX DIAGNOSIS
AND MEDICAL TREATMENT.
AU DALESSIO D J [Reprint author]
CS DEP MED, SCRIPPS CLIN RES FOUND, LA JOLLA, CALIF 92037, USA
SO (1982) pp. P135-144. BRACKMANN, D. E. (ED.). NEUROLOGICAL SURGERY OF THE
EAR AND SKULL BASE. XIX+408P. RAVEN PRESS: NEW YORK, N.Y., USA. ILLUS.

TI Tic douloureux and diabetes mellitus.
AU Collis J S Jr; Wallace T W
SO CLEVELAND CLINIC QUARTERLY, (1968 Jul) 35 (3) 155-7.
Journal code: 0373162. ISSN: 0009-878

TI Trigeminal glycerol rhizolysis in the treatment of tic
douloureux.
AU Rappaport Z.H.; Magora F.
CS Department of Neurosurgery, Hadassah University Hospital, Ein- Kerem,
Jerusalem, Israel
SO European Journal of Anaesthesiology, (1985) 2/1 (53-57).

TI [Trigeminal neuralgia. Possibility of treating the pain with
transcutaneous nerve block].
TRIGEMINUSNEURALGIE. SCHMERZBEKAMPFUNG DURCH TRANSKUTANE NERVENBLOCKADE.
AU Artnet F.
CS Ambulat. f. Phys. Medizin u. Rehab., Burgenländische Gebietskrankenkasse,
A-7001 Eisenstadt, Austria
SO Fortschritte der Medizin, (1986) 104/38 (711-714). English version.

TI Benign chronic orofacial pain. Clinical criteria and therapeutic
approaches.
AU Dworkin S.F.
CS Dep. Oral Med., Univ. Washington SC-63, Seattle, WA 98195, United States
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I Pain relief from peripheral conditioning stimulation in patients
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AU Eriksson M B; Sjolund B H; Sundbarg G
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Journal code: 0253357. ISSN: 0022-3085.

Vanessa L. Ford

Facial Nerve Pain Excluding Tic Douloureux: Diagnosis and Medical Treatment

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EVALUATION OF THE PATIENT WITH CHRONIC FACIAL PAIN

The physician confronted by the patient with chronic facial pain should establish a diagnosis as soon as possible. The work-up should use non-invasive techniques for examination of the cranial and facial contents.

To successfully establish a diagnosis, a working classification of facial pains is necessary. Table 1 lists six main groups of facial pains: vascular, muscular, neuritic, rheumatic, traction and inflammatory, and psychogenic.

Some diagnoses can be suspected on the basis of history alone, including migraine and other forms of paroxysmal recurrent headache, the major neuralgias, and various psychogenic head pains. Furthermore, the proper use of this classification system leads naturally to considerations of therapy.

CLUSTER HEADACHE

Cluster headache is characterized by recurrent unilateral attacks of headache of high intensity and brief duration (1—3). The attacks are often accompanied by symptoms and signs such as redness and tearing of the eye and stuffiness of the nose on the same side as the pain. Perhaps the most notable feature is the clustering of the attacks. Generally they occur in 6-week cycles; sometimes they occur annually. Prolonged periods of relief from headache are characteristic. There are no prodromata. Pain is often excruciating within minutes after onset, and pain frequently wakes the patient after a few hours of sleep. A unilateral partial Horner's syndrome may occur after repeated attacks. Headaches may occur just after periods of intensive dreaming, during the so-called "rapid eye movement" sleep.

Cluster headache is largely a disease in men: 80 to 90% of patients with this complaint are males. Age of onset is between 20 and 40 years. Patients are extremely sensitive to vasodilating agents during the course of the cluster headache phase.

TABLE 1. Classification of chronic facial pains and neuralgias

Vascular	Muscular	Neuritic	Rheumatic	Psychogenic	Traction and Inflammatory
A. Paroxysmal recurrent 1. Migraine a. Classic b. Common c. Complicated 2. Cluster 3. Lower half 4. Raeder's syndrome B. Toxic/Metabolic C. Hypertensive D. Arterial, degenerative 1. Atheromatous 2. Embolic 3. Aneurysmal 4. Arterial venous malformation 5. Transient ischemic attack E. Arteritis, cranial 1. Giant cell 2. Granulomatous/infectious 3. Immune complex 4. Tolosa-Hunt F. Thrombophlebitis G. Carotidynia H. Obscure	A. Myositis B. Fibromyalgias C. Neoplastic	A. Paroxysmal 1. Trigeminal neuralgia 2. Glossopharyngeal 3. VII, X nerve neuralgias 4. Occipital B. Chronic 1. Post-traumatic 2. Post-herpetic 3. Toxic 4. 2° collagen disease	A. Temporomandibular joint disease B. Infections C. Neoplastic	A. Burning tongue and mouth B. Atypical facial pains C. Conversion reactions D. Depressive equivalents	A. Mass lesions B. Diseases of eye, ear, nose, throat, and teeth 1. Infections 2. Degenerative 3. Edematous 4. Neoplastic

Headaches can be triggered by

of the patients are heavy smokers. The etiology of cluster headache is exclusively in males who smoke. However, we have been unable to expose these patients to tobacco or its products. Nor do these patients have positive tests. Their Lewis triple response to strychnine is normal. Although other histamine in the blood of patients with cluster headache assay technique has not been able to detect elevated levels.

We are impressed, however, with the value of the syndrome. This ganglion, located in the orbit, receives sympathetic efferents from the cell bodies of the palatine nerve, the greater superficial petrosal nerve, the vidian canal. It receives sympathetic afferents via the deep petrosal nerve, which is a branch of the vidian nerve. It receives afferents from the periosteum of the orbit. Electrochemical stimulation produces a syndrome much like the sphenopalatine ganglion in heavy smokers. It becomes hyperactive, usually on exposure to stimuli may thereafter trigger attacks.

Treatment may be prophylactic or symptomatic. It is difficult to treat since prodromal symptoms may awaken the patient from sleep, and the attack is short-lived. Medications that inhibit the secretion or actions of vasoactive substances, such as methysergide 3 times daily and alcohol containing vasoactive substances, may be used at 6 to 9 L/min. If medications are ineffective, the rationale for their use is not clear. The effects on inflammation. Prednisone has been effective. As the headache subsides, the medication is finally discontinued. In an occasional case, the headache is a treatment problem of significant duration. Prolonged periods of time because of the headache may be used. A few patients may require amounts to produce remission of the headache.

Surgical treatment of typical cluster headache problem becomes chronic, local anesthetic cocaine can be tried 2 or 3 times.

The etiology of cluster headache remains an enigma. Symptoms recur almost exclusively in males who smoke heavily. This suggests some possible precipitating factors. However, we have been unable to demonstrate any unusual reaction in these patients to tobacco or its products, as determined by intradermal challenge tests. Nor do these patients have unusual or exaggerated signs of histamine release. Their Lewis triple response to stroking of the skin is not increased, and their response to substances that provoke the release of histamine is not different from that of normal controls. Although other investigators have found increased amounts of histamine in the blood of patients with cluster headache, our use of a sensitive bioassay technique has not been able to confirm this finding.

Treatment may be prophylactic and abortive (Tables 2 and 3). Acute attacks are difficult to treat since prodromal symptoms are frequently lacking, the pain may awaken the patient from sleep, and the pain attains its maximum intensity rapidly and is short-lived. Medications that reduce vascular activity and inhibit the elaboration or actions of vasoactive amines are effective. Frequently we use 2 mg of methysergide 3 times daily and 8 mg of cyproheptadine at bedtime. Foods and alcohol containing vasoactive substances should be avoided. Oxygen may be used at 6 to 9 L/min. If medications are not effective, corticosteroids should be added. The rationale for their use is not clear but is probably related to their multiple effects on inflammation. Prednisone 30 mg every other day for 10 to 14 days has been effective. As the headache ends, the medications are gradually reduced and finally discontinued. In an occasional patient, chronic cluster headaches appear and are a treatment problem of significance. Methysergide should not be used for prolonged periods of time because of its tendency to produce fibrosis. Cyproheptadine may be used. A few patients have been treated with lithium in adequate amounts to produce remission of the headaches for weeks to months.

Surgical treatment of typical cluster headache is almost never necessary. If the problem becomes chronic, local infiltration of the sphenopalatine ganglion with cocaine can be tried 2 or 3 times weekly as long as symptoms persist. If this

- E. Arteritis, cranial
 1. Giant cell
 2. Granulomatous/
 infectious
 3. Immune complex
 4. Tolosa-Hunt
 F. Thrombophlebitis
 G. Carotidynia
 H. Obscure

TABLE 2. Abortive cluster therapy treatment

Route	Drug	Dosage
Oral	Ergotamine tartrate (Gynergen [®])	One tablet immediately. Repeat every ½ hour if necessary. Maximum of 6 tablets per day.
	Ergotamine, caffeine, phenacetin, belladonna (Wigraine [®])	2 stat. Repeat one every ½ hour. Maximum of 6 per day.
	Ergotamine and caffeine (Cafertog [®])	2 tablets at onset. May repeat one tablet every ½ hour up to 6 per day.
	Ergotamine tartrate, cyclizine, and caffeine (Migral [®])	One tablet immediately under the tongue. Repeat at ½ hour intervals if necessary, but not more than 3 in any 24-hour period.
	Ergotamine (Ergomar [®] , Ergostat [®])	One dose immediately. Repeat every 5 minutes to a maximum of 6 per day, if necessary.
Sublingual	Ergotamine (Medihaler-Ergotamine)	By nasal mask, 6 to 9 liters/min for 10 to 15 min.
Inhalation	Oxygen	½ to 1 cc immediately and no more than 3 cc per week.
Intramuscular	Ergotamine tartrate (Gynergen [®])	1 cc at hourly intervals, up to 3 cc per day, if necessary.
Rectal	Dihydroergotamine (DHE 45 [®])	
	Ergotamine and caffeine (Cafertog-PB [®])	Insert 1 suppository in rectum immediately. Repeat in one hour, if necessary.

TABLE 3. Pro

Drug
Methysergide maleate (Sanser)
Triamcinolone (Aristocort [®])
Methylprednisolone (Medrol Ate)
Cyproheptadine (Periactin [®])
Ergotamine, phenobarbital, and
Bellergal [®] Spacetabs
Bellergal [®]
Lithium (Eskalith [®])

procedure consistently relieve the sphenopalatine ganglion.

DISEASES OF THE

Facial pain may, of course, The clinician should check for plasm. Use of computerized to in these areas easier, particular the like. An ear, nose, and suspected of having chronic s upon the nose or sinuses are to pain and if no obvious disease or turbinates should not be co

In evaluation of patients with a dentist well trained in oral dis dental pain crosses the midline the pain is probably not dental facial pain. The problem of te

Cranial arteritis is a febrile, and females. It is characterized cranial arteries and generalized weakness, weight loss, anore cranial arteritis have headache aching, throbbing in nature, a The headache is frequently we by the upright position. It ma the artery involved. Often the artery may be enlarged an greatly increases pain. Some p

TABLE 3. Prophylactic (oral) cluster therapy treatment

Drug	Dosage
Methysergide maleate (Sansert®)	2 mg 3 times daily
Triamcinolone (Aristocort®)	4 mg 4 times daily; 16 mg every other day
Methylprednisolone (Medrol Alternate Day Therapy Pac®)	4 mg 4 times daily
Cyproheptadine (Periactin®)	8 mg at bedtime
Ergotamine, phenobarbital, and belladonna	
Bellergal® Spacetabs	one tablet twice daily
Bellergal®	one tablet 3 to 4 times daily
Lithium (Eskalith®)	900 mg per day

procedure consistently relieves pain, the patient may benefit from cryotherapy of the sphenopalatine ganglion.

DISEASES OF THE EYE, EAR, NOSE, AND THROAT

Facial pain may, of course, be related to diseases of other structures of the head. The clinician should check for glaucoma, sinusitis, arteritis, inflammation, or neoplasm. Use of computerized tomography and the body scanner will make diagnosis in these areas easier, particularly if one is concerned about retro-orbital tumors and the like. An ear, nose, and throat consultation should be obtained for patients suspected of having chronic sinusitis. In general, however, extensive operations upon the nose or sinuses are to be avoided, particularly if the complaint is chronic pain and if no obvious disease is evident. Minor abnormalities of the nasal septa or turbinates should not be corrected unless there is another reason for doing so.

In evaluation of patients with possible dental disease, consultation should be with a dentist well trained in oral diseases. It is important to know, for example, whether dental pain crosses the midline or if it is unresponsive to local anesthesia. If so, the pain is probably not dental. Good teeth should not be removed for reasons of facial pain. The problem of temporomandibular joint disease is discussed later.

Cranial Arteritis

Cranial arteritis is a febrile, often self-limited disease that affects elderly males and females. It is characterized by painful inflammation of the temporal and other cranial arteries and generalized systemic signs and symptoms including malaise, weakness, weight loss, anorexia, fever, and sweating (4). Not all patients with cranial arteritis have headache, but when present it is of high intensity, deep and aching, throbbing in nature, and persistent. There is often a burning component. The headache is frequently worse when the patient lies flat and may be improved by the upright position. It may be exacerbated or reduced by digital pressure on the artery involved. Often there is associated hyperalgesia of the scalp. Occasionally the artery may be enlarged and distended and extremely tender, so that pressure greatly increases pain. Some patients may suffer pain on mastication or with move-

day, if necessary.
By nasal mask, 6 to 9 liters/min for 10 to 15 min.
1/2 to 1 cc immediately and no more than 3 cc per week.
1 cc at hourly intervals, up to 3 cc per day, if necessary.

Oxygen
Ergotamine tartrate (Gynergen®)
Dihydroergotamine (DHE 45®)
Ergotamine and caffeine (Cafergol,
Cafergol-PB®)
Ergotamine, caffeine, phenacetin,
belladonna (Wigraine®)

Insert 1 suppository in rectum immediately. Repeat in one hour, if necessary.

ments of the jaw producing a type of jaw claudication. Pain may also be at the back of the head or in the tongue. Symptoms may involve any of the primary divisions of the external carotid artery. Other arteries may also be involved including the major vessels of the aorta, of the limbs, and the coronaries.

An important presenting complaint in this syndrome is loss of vision (5). Perhaps one-third to one-half of patients with cranial arteritis are threatened with partial or even complete loss of vision. If loss of vision is the presenting complaint, the patient is a medical emergency requiring urgent treatment. Treatment should not wait until temporal artery biopsy is used for the diagnosis. Prednisone or some other corticosteroid is the treatment of choice, and 40 to 60 mg should be given as soon as the diagnosis is made. The sedimentation rate should be followed to guide management with prednisone. A low maintenance dose of approximately 10 to 20 mg is usually necessary for a prolonged time.

TEMPOROMANDIBULAR JOINT DISEASE

The temporomandibular joint (TMJ) is the only movable joint in the head, excluding the junction of the head with the atlas. Disease of the temporomandibular joint is relatively rare. The most common complaint in TMJ disease is headache, of moderate intensity, located at the vertex, occiput, or in the face overlying the joints. Diagnosis is sometimes difficult. One should certainly palpate and auscultate the joints with significant pressure and with the patient's opening and closing his mouth. If crepitus can be heard, osteoarthritis in the joint can be assumed. Then a local anesthetic, such as 1 cc of a 2% solution of lidocaine, can be injected into the joint to determine if it alters facial pain. Here again, consultation with a dentist who is knowledgeable in this field is essential (5). Patients with temporomandibular joint disease have pain primarily from muscular tension related to dental occlusive disease. Because of localized pain, the patient begins to use the opposite side of the mouth for chewing, attempting to splint the painful side, but, in fact, this has exactly the opposite effect and makes the painful joint do all the work. For example, with right temporomandibular joint disease, chewing on the left side moves the right temporomandibular joint excessively. The treatment in this situation should invariably be conservative, with use of occlusive equilibration, splints, physical therapy, and correct chewing techniques, all calculated to reduce muscle spasm and fatigue. These patients should not have surgery if possible. Reconstruction of the joint is indicated only in the rare instance when organic disease of the joint itself can be demonstrated.

ATYPICAL FACIAL NEURALGIAS

The term "atypical facial neuralgias" is used for pain syndromes that cannot be otherwise categorized, that are not associated with trigger zones, and in which a steady, diffuse, aching pain of hours' to days' duration occurs, which is not paroxysmal, and in which no consistent history can be obtained. Multiple factors may be responsible for the production of this complaint. A careful search should be

made for local pathology of the c patients with atypical facial pains. common migraine involving the fac A trial of a vasoconstrictor agent o systems including cutaneous pallor involved, attempts to alter respon blockers, such as propranolol, can standing, atypical facial pains requi to the problem is indicated to ident or otherwise, to isolate factors co measure the severity of the pain th chological testing and pain measure pain-relieving or analgesic medicat ications, nerve blocks, electrical n duction of muscle spasm, activity always be sensible and pragmatic.

POST-INFEC

The pain of herpes zoster, partic face, often dominates the waning ularly intense, long-lasting, and as interrupts sleep at night and produ and all problems of chronic pain, it are extremely difficult to treat. Med particularly the tricyclic antidepress neurostimulation of the skin surfac may be efficacious, but this is rar ablative surgical procedures are us patience, counseling, and reassuran that no treatment is likely to be cu

RAEDER'S SYNDROME A

Raeder's paratrigeminal syndrom sympathetic paralysis, the sudden pain of rapid onset with associated tribution, no previous history of he area of the ipsilateral forehead. Rae cranial nerve dysfunctions, usually geminal, and abducens nerves. Rae region of the trigeminal ganglion a of his cases had multiple cranial ne head injury. In 2 cases no particul Raeder's patients had multiple cra

on. Pain may also be at the back of the head. Any of the primary divisions of the trigeminal nerve may also be involved including the ophthalmic division.

One is loss of vision (5). Perhaps the cornea is threatened with partial or total blindness as the presenting complaint, the treatment. Treatment should not be given until a definite diagnosis. Prednisone or some other corticosteroid. 40 to 60 mg should be given as a starting dose and should be followed to guide the patient. A dose of approximately 10 to 20 mg per day.

TMJ DISEASE

A movable joint in the head, a disease of the temporomandibular joint in TMJ disease is headache, pain, or in the face overlying the joint. The patient should certainly palpate and auscultate the joint during the patient's opening and closing his mouth. The joint can be assumed. Then a local anesthetic, such as lidocaine, can be injected into the joint.

Patients with temporomandibular dysfunction related to dental occlusive problems may begin to use the opposite side of the mouth for chewing on the painful side, but, in fact, this has not done all the work. For example, chewing on the left side moves the mandible to the right. Treatment in this situation should be conservative, splints, physical therapy, and relaxation to reduce muscle spasm and if possible. Reconstruction of the joint is not the organic disease of the joint itself.

NEURALGIAS

For pain syndromes that cannot be relieved with trigger zones, and in which a definite duration occurs, which is not permanent, a diagnosis may be obtained. Multiple factors may be involved. A careful search should be made for local pathology of the eyes, nose, teeth, sinuses, and pharynx. Some patients with atypical facial pains may be suffering from a form of vascular or common migraine involving the face, particularly if the pain is throbbing in nature.

A trial of a vasoconstrictor agent of the ergot type may be helpful. If autonomic systems including cutaneous pallor, sweating, flushing, rhinitis, and the like are involved, attempts to alter responses to autonomic stimuli with beta-adrenergic blockers, such as propranolol, can be employed. Many patients with chronic, long-standing, atypical facial pains require intensive inpatient evaluation. This approach to the problem is indicated to identify, if possible, the origins of the pain, medical or otherwise, to isolate factors contributing to the problem, and to quantify or measure the severity of the pain the patient is experiencing. In this situation psychological testing and pain measurements should be included. Treatment can include pain-relieving or analgesic medications, attitude-influencing or psychotropic medications, nerve blocks, electrical neurostimulation, biofeedback techniques for reduction of muscle spasm, activity management, and family counseling. It should always be sensible and pragmatic.

POST-INFECTIOUS NEURALGIAS

The pain of herpes zoster, particularly the postherpetic pain in the forehead and face, often dominates the waning years of elderly individuals. The pain is particularly intense, long-lasting, and associated with severe dysesthesias. It frequently interrupts sleep at night and produces reliance on habituating drugs, depression, and all problems of chronic pain, including consideration of suicide. Such patients are extremely difficult to treat. Medications that influence attitudes may be helpful, particularly the tricyclic antidepressants combined with a phenothiazine. Electrical neurostimulation of the skin surface of the area involved by the herpes infection may be efficacious, but this is rarely possible when the face is involved. Local ablative surgical procedures are usually not helpful. Generally the patient requires patience, counseling, and reassurance. He or she also needs to acquire understanding that no treatment is likely to be curative.

RAEDER'S SYNDROME AND THE PERICAROTID SYNDROME

Raeder's paratrigeminal syndrome (6) is a rare illness characterized by oculosympathetic paralysis, the sudden onset of severe frontotemporal burning, aching pain of rapid onset with associated ptosis and meiosis, often in a periorbital distribution, no previous history of headache, and normal sweating in the supraorbital area of the ipsilateral forehead. Raeder based his conclusions on 5 patients, all with cranial nerve dysfunctions, usually involving the optic, oculomotor, trochlear, trigeminal, and abducens nerves. Raeder's first patient had a tumor arising from the region of the trigeminal ganglion and infiltrating all of these cranial nerves. Two of his cases had multiple cranial nerve lesions and sympathetic paralysis related to head injury. In 2 cases no particular cause could be identified. In essence, then, Raeder's patients had multiple cranial nerve involvements, primarily parasellar,

associated with oculosympathetic paralysis and intact facial sweating. Others have since used the term "Raeder's syndrome" to describe almost any lesion producing oculosympathetic paralysis associated with head pain. It is probably better precisely to classify patients with oculosympathetic paralysis and headaches with or without disturbances of sweating as well.

Many patients with cluster headaches have an associated oculosympathetic paralysis. In this case the tempo of the cluster headache, rather than the autonomic dysfunction, establishes the diagnosis.

Vijayan and Watson (9) described a pericarotid syndrome characterized by oculosympathetic paralysis, ipsilateral head pain, and anhidrosis over the forehead with otherwise intact facial sweating. They suggest that the site of the lesion involving the oculosympathetic fibers in their patients is pericarotid. Their patients had no previous history of headache. They were able to establish a pathogenesis in only one of their 6 patients who had a left internal carotid artery occlusion. In the other 5 patients, the etiology was unknown (8,9).

FACIAL PAIN AND DIABETIC NEUROPATHY

Isolated cranial nerve palsies, especially of the third and sixth nerves, occur in diabetes. Neuralgia of the fifth nerve with diabetic ocular paresis may occur.

No explanation for the pain or its rarity is available. It appears likely that the third, fourth, and sixth cranial nerve defects stem from vascular occlusive disease of the vasa nervorum, and that the fifth cranial nerve may rarely become similarly involved.

SUMMARY

Perhaps no subject in medicine is as confusing to patient and physician alike as recurrent chronic facial pain. Frequently unilateral, often unresponsive to therapy, long-lasting, and discomforting, chronic facial pains have resisted even simple nosologic classifications. This paper proposes classification of chronic facial pains.

The physician who understands how to deal with patients in chronic pain and who understands the mechanisms behind pain-centered behavior may be able to improve significantly the life of many of these patients by judicious use of a combination of drug therapies, behavioral techniques, physical therapy, and the like. Here, as elsewhere in medicine, patience and perseverance on the part of the physician are probably more important than pharmacological knowledge or surgical technique.

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NEUROPATHY

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CS Dep. Neurol., Barrow Neurol. Inst., 350 W. Thomas Rd., Phoenix, AZ 85013, USA

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Journal code: 7507211. ISSN: 0021-1133.

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Uses of botulinum toxin

SIR—Naumann and colleagues (Jan 25, p 252)¹ describe a patient with continuous excessive sweating of the palms who was treated effectively with intracutaneous injection of botulinum toxin (BTX). Several workers have suggested the use of BTX in the management of focal hyperhidrosis.^{2,3} We did a randomised double-blind trial to study the effect of subcutaneous injections of BTX in palmar hyperhidrosis.⁴ Objective measurement as well as subjective rating showed reduction of sweat production in the botulinum-treated hand compared with the placebo-treated hand.

We subsequently treated seven patients (two women, five men, aged 23–35 years) with palmar hyperhidrosis with subcutaneous BTX. All patients were resistant to any conventional treatment. The study was approved by the ethics committee of the University of Vienna medical faculty. We sought to determine the duration of anhydrotic effect, individual satisfaction, and the extent of weakness in the small hand muscles after injections of BTX. Ninhydrin sweat tests were done before injections to visualise the areas of most intense sweating. At weekly intervals the patients were asked to rate the intensity of sweat production using a visual analogue scale (VAS: 0=no sweating; 100=most severe) and to rate their satisfaction with treatment (very effective; effective; moderate; no effect). Side-effects were documented by a structured checklist. Sustained muscle power of the hand muscles was tested for four different movements by squeezing a blood pressure cuff between fingers I and II, fingers II and III, fingers I and V, and hand grip before treatment and at monthly intervals. BTX was injected subcutaneously into the most hyperhidrotic areas. 10 mU or 20 mU BTX (500 mU diluted in 1.25 mL saline 0.9%) were injected per site. A mean total dose of 188.1 (SD 66.8) mU BTX for both palms was injected at a single treatment session. Repeated injections were given after 1 month in case of incomplete treatment response (three patients), or at subsequent follow-up visits when the anhydrotic effect was lost, rated by subjective assessment (four patients). The mean observation period was 9.1 months (range 8–12 months). Subjective rating of sweating improved from 79.3 mean VAS (SD 17.7) before to 26.5 mean (SD 8.5) 6 weeks after treatment. Two patients rated treatment as very effective and five as effective. The mean duration of anhydrotic effect was 5.6 months (range 2–10 months). Apart from subjective weakness of handgrip in two patients lasting 4 days and 3 weeks, respectively, no other side-effects were reported. Muscle power testing,

however, revealed weakness in three of seven patients (sustained muscle power reduced to <50%) for grip between fingers I and V, lasting up to 8 weeks.

The management of palmar hyperhidrosis is controversial. Topical antiperspirants and iontophoresis are only effective in the mildest cases. Sympathectomy is usually effective and longlasting but may be complicated by surgical risks, cosmetic problems, and compensatory hyperhidrosis.¹ BTX blocks the release of acetylcholine at the neuromuscular junction, and also in postganglionic sympathetic cholinergic fibres to sweat glands. Although our results confirm the effectiveness of BTX in treating focal hyperhidrosis, weakness of the small hand muscles could be a limiting factor for this new treatment.

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Harald Kittler, Nikolaus Steinhoff,
Eduard Auff

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SIR—Naumann and Brin and colleagues describe the therapeutic use of botulinum toxin. It is astonishing that one of the most lethal biological toxins known to man is proving to have increasing therapeutic value. The ability of this toxin to produce chemical denervation of muscle means that it has exciting potential use in many neuromuscular and ophthalmic disorders.

We have used botulinum toxin to successfully alleviate the debilitating facial pain that arises from the chronic muscle spasm of facial arthromyalgia. This condition afflicts over 25% of the population at some stage of their life. Spasm in the muscles of mastication leads to trismus, facial pain, and limitation of jaw function.⁴ Although of huge importance to dental, oral, and maxillofacial surgeons this condition is poorly recognised by rheumatologists and orthopaedic specialists. Current treatment options including bite guards, anti-inflammatory analgesics,

physiotherapy, tricyclic antidepressants, and surgery have a variable success rate.

We obtained informed consent from a 34-year-old man with a 6-year history of facial arthromyalgia that was unresponsive to standard treatment. 250 units of botulinum toxin type A (Dysport, Speywood Pharmaceuticals Ltd, Maidenhead, UK), dissolved in 1.25 mL saline, were injected into the bulk of each masseter muscle. The solution was dispersed by massaging the muscle for 20 minutes. At review 10 days later the patient reported minor discomfort and bruising for 24 h, followed 48 h later by complete cessation of facial pain. Jaw function had improved dramatically and he had been able to eat his first pain-free meal for 6 years. At 6-month review the patient still had painless jaw function and there were no signs of recurrent muscle spasm or joint dysfunction.

Botulinum toxin prevents acetylcholine release and causes functional neuromuscular denervation. It temporarily paralyses the affected muscle and provides relief from the pain of chronic muscle spasm. This treatment could give relief to patients with intractable facial arthromyalgia that has failed to respond to standard management regimens.

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Newcastle Dental School and Hospital, Royal Victoria Infirmary and Associated Hospitals NHS Trust, Newcastle upon Tyne NE2 4AZ, UK

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Differing proteinuria control with cyclosporin and tacrolimus

SIR—Budde and colleagues (Feb 1, p 330)¹ report a renal transplant recipient with recurrent membranoproliferative disease type I, in whom cyclosporin rather than tacrolimus controlled severe proteinuria. This finding is unexpected, since McCauley and colleagues² reported that six of ten patients with new or recurrent focal sclerosing glomerulonephritis in kidney transplants responded to conversion from cyclosporin to tacrolimus with a reduction of proteinuria of more than 50% (reduction of proteinuria from 7.2 g to

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AU DALESSIO D J [Reprint author]
CS DEP MED, SCRIPPS CLIN RES FOUND, LA JOLLA, CALIF 92037, USA
SO (1982) pp. P135-144. BRACKMANN, D. E. (ED.). NEUROLOGICAL SURGERY OF THE
EAR AND SKULL BASE. XIX+408P. RAVEN PRESS: NEW YORK, N.Y., USA. ILLUS.

TI Tic douloureux and diabetes mellitus.
AU Collis J S Jr; Wallace T W
SO CLEVELAND CLINIC QUARTERLY, (1968 Jul) 35 (3) 155-7.
Journal code: 0373162. ISSN: 0009-878

TI Trigeminal glycerol rhizolysis in the treatment of tic
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CS Department of Neurosurgery, Hadassah University Hospital, Ein- Kerem,
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A-7001 Eisenstadt, Austria
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approaches.
AU Dworkin S.F.
CS Dep. Oral Med., Univ. Washington SC-63, Seattle, WA 98195, United States
SO Postgraduate Medicine, (1983) 74/3 (239-248).

I Pain relief from peripheral conditioning stimulation in patients
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AU Eriksson M B; Sjolund B H; Sundbarg G
SO JOURNAL OF NEUROSURGERY, (1984 Jul) 61 (1) 149-55.
Journal code: 0253357. ISSN: 0022-3085.

Vanessa L. Ford

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e oxidase inhibitor. *J. A. M. A.* 193: 1-6, 1965.

Tic douloureux and diabetes mellitus

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Department of Neurologic Surgery

THOMAS W. WALLACE, M.D.

Department of Neurology

THE facts that tic douloureux is an extremely painful disorder and that diabetes mellitus is frequently associated with pain at varied sites, led us to explore a possible association between the two disease entities. Accordingly, 30 patients with tic douloureux, whose status in regard to possible diabetes mellitus was not known, were selected for the study.

PATIENTS

All 30 patients had typical idiopathic tic douloureux with pathognomonic pain. In no patient were there significant abnormal neurologic signs.

All of the patients were tested for glucose tolerance. The glucose tolerance tests consisted of blood sugar determinations both one hour and two hours after a 100-g glucose meal. The upper limits for the one-hour and two-hour blood sugar values were 160 mg and 105 mg per 100 ml, respectively. Of the 30 patients, 10 had abnormal values in the diabetic range. The case data are summarized in *Table I*.

COMMENT

Many pathologic conditions have been associated with tic douloureux. These include multiple sclerosis, brain tumors, and vascular anomalies. Likewise, many abnormal conditions have been associated with diabetes mellitus.

However, published reports have not mentioned that diabetes mellitus was associated with tic douloureux.¹ Though the number of patients in our series is small, the proportionately large number of patients with abnormal results of glucose tolerance tests, in the diabetic range, we believe is significant.

Possible sources of error were explored before we drew conclusions. For example, a period of starvation can produce abnormally high blood sugar values.² It is certainly well known that patients suffering from tic douloureux will avoid eating during painful paroxysms, or may not eat in order to avoid pain. Also, pain, or anticipation of it, may cause an increase in circulating epinephrine, which in turn can increase the blood sugar value.

Table 1.—Summary of the data of 10 patients with tic douloureux and abnormal results of glucose tolerance tests

Patient	Age, yr	Sex	Site of facial pain: side, division	Blood glucose content (after 100-g glucose meal), mg/100 ml		Glucosuria present	Diabetic relatives
				1 hr*	2 hr†		
1	58	F	Left, third	202	153	No	None
2	60	F	Left, second and third	170	100	No	Mother
3	61	F	Left, second and third	178	179	No	None
4	64	M	Right, second	270	246	Trace	Not known
5	68	F	Right, second and third	167	116	No	Nephew's two children
6	69	M	Right, first and second	188	112	Not known	None
7	72	F	Right, second and third	246	270	Not known	None
8	75	F	Left, first and second	202	172	No	None
9	77	M	Right, first, second and third	303	208	Trace	Not known
10	91	M	Right, first and second	163	159	No	None

* Upper limit, 160 mg/100 ml.

† Upper limit, 105 mg/100 ml.

Both possible conditions are not likely to be applicable to the 30 patients, because abnormal blood sugar values were found in a few patients who were not limited as to diet, and in whom surgical relief of pain had been obtained.

It may be entirely possible that tic douloureux is a symptom of diabetes mellitus. Recognition of this possibility may lead to a better understanding both of tic douloureux and of diabetes mellitus, and hence to more precise treatment of both entities.

This report is thought to be the first to demonstrate an association of diabetes mellitus and tic douloureux.

CONCLUSION

Tic douloureux may be a symptom of diabetes mellitus. Of 30 patients with tic douloureux, whose blood sugar values were not previously known, 10 had abnormally high values, in the range of those of patients

with diabetes mellitus. We believe presented as demonstrating an association. We suggest that patients with tic douloureux to diabetes mellitus is not known. We suggest that patients with tic douloureux to diabetes mellitus is not known. We suggest that patients with tic douloureux to diabetes mellitus is not known.

1. Structural aspects of trigeminal neuralgia. Jannetta, P., and others. J. Neurosurg. 1950; 42: 382-390.
2. Conn, J. W.: The spontaneous hypoglycemia. J.A.M.A. 115: 1669-1675, 1936.

WALLACE

Patients with tic douloureux and abnormal tolerance tests

Fasting glucose tolerant (after -g glucose meal), g/100 ml		Glucosuria present	Diabetic relatives
* 2 hr†			
153	No	No	None
100	No	No	Mother
179	No	No	None
246	Trace	No	Not known
116	No	No	Nephew's two children
112	Not known	No	None
270	Not known	No	None
172	No	No	None
288	Trace	No	Not known
159	No	No	None

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DISCUSSION

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TIC DOULOUREUX AND DIABETES MELLITUS

with diabetes mellitus. We believe that the 10 cases are the first to be presented as demonstrating an association of diabetes mellitus and tic douloureux. We suggest that patients with tic douloureux, whose status in regard to diabetes mellitus is not known, be given glucose tolerance tests to establish the presence or absence of diabetes mellitus.

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Trigeminal glycerol rhizolysis in the treatment of tic douloureux

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Accepted 4 February 1984

SUMMARY

Eleven patients suffering from trigeminal neuralgia were treated by percutaneous glycerol trigeminal rhizolysis after visualization of the trigeminal cistern with metrizamide. In 10 of 11 cases treatment was successful and the pain disappeared. The technique of the treatment is described. This form of treatment is recommended as a successful and simple method, especially in the elderly population suffering from trigeminal neuralgia.

Trigeminal neuralgia is a common ailment, especially among the elderly, which is characterized by lightning-type pain attacks in the face. The pathophysiology of the disease is thought to be related to partial demyelination of the trigeminal nerve root giving rise to ephaptic contacts between fibres.¹ Anatomical variants and vascular compression of the nerve root entry zone, tumour, and multiple sclerosis have been cited as other possible causes.² The mainstay of treatment of this condition is drug therapy (e.g. carbamazepine). In about half of the patients, however, poor tolerance or continuing pain have necessitated interventional therapy.³

Most surgical approaches, while providing long-lasting pain relief, produce some sensory deficit. Neuro-ablative procedures entail the risk of dysaesthesia and anaesthesia dolorosa. Percutaneous radiofrequency trigeminal rhizolysis has been widely accepted as a successful form of therapy of tic douloureux.⁴ The resulting graded differential thermal lesion generally preserves touch sensation. However, for longer lasting, more effective lesions, there is a risk of paraesthesia and even, in up to 2% of cases, anaesthesia dolorosa.⁵ Glycerol injection into the trigeminal cistern has been reported to provide effective pain relief for patients suffering from tic douloureux, without causing significant sensory abnormalities or dysaesthesia.^{6,7} Following a visit to Dr Hakanson in Stockholm, one of us (ZHR) has begun to use this technique in selected cases. A report of the methodology used and the results obtained is presented.

METHOD

A point, 3 cm lateral to the angle of the mouth on the side of the pain is cleaned and anaesthetized with 1% lignocaine. A radio-opaque marker is placed at this spot and is lined up with the foramen ovale, as demonstrated by fluoroscopy, by extending and rotating the head. A 22 G, 100 mm needle is then introduced into the skin perpendicularly at the site of the marker, under fluoroscopic control (Fig. 1). Passage through the dura will usually be felt by the operator. Once a free flow of CSF is obtained the patient is placed in the sitting position and a small quantity of metrizamide (300 mg%) is introduced. X-rays are taken in A-P and lateral projection to identify Meckel's cave and to rule out a needle placement which is too deep or subtemporal (Fig. 2). The volume of the trigeminal cistern is noted. It will vary between 0.2 and 0.7 ml. In cases of V_2 and/or V_3 trigeminal neuralgias the metrizamide is allowed to escape and some pure glycerol (0.2–0.5 ml) is injected as determined by the trigeminal cisternography. In the case of solitary V_1 involvement, the metrizamide is only half drained, and the glycerol is allowed to float to the upper portion of the cistern where it will be in contact with the ophthalmic division fibres. The needle is then removed. The patient must remain seated for an hour to prevent premature escape of the glycerol.

RESULTS

Using this method, we have treated 11 patients with trigeminal neuralgia, a number of whom had undergone multiple peripheral trigeminal neuroablative procedures in the past (Table 1). All patients had undergone radiological evaluation including computerized tomography to exclude a tumour. The average age of the patients was 66 years. The trigeminal divisions were as follows: four patients with V_2 , two patients with V_3 , two patients with $V_{2,3}$, two patients with $V_{1,2}$ and one patient with $V_{1,2,3}$ pain. Eight of the cases involved the right side of the face and three were on the left. The group consisted of eight men and three women. Two cases of atypical trigeminal neuralgia were included in the case material. Ten of 11 patients had virtually complete pain relief in the time between immediately postoperatively (five patients) and up to 7 days postoperatively. One patient with atypical facial pain had no relief of symptoms

Table 1. Multiple peripheral trigeminal neuro-ablative procedures.

Prior forms of therapy	no. of patients
Extraction of teeth	9
Alcohol blocks of peripheral nerve	5
Neurectomies	2
Posterior fossa exploration	1
Psychiatric treatment	2
Treatment with carbamazepine	11

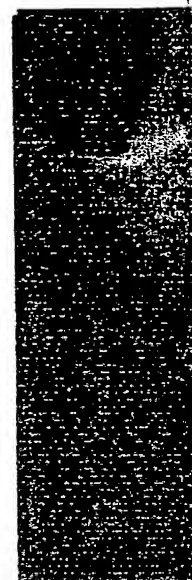


Fig. 1. A radio-opaque marker (small white dot) and spinal needle penetrates the foramen ovale.



Fig. 2. Metrizamide filling the trigeminal cistern.

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Fig. 1. A radio-opaque marker (scalpel blade) is superimposed over the foramen ovale. A spinal needle penetrates the foramen ovale in a perpendicular direction.

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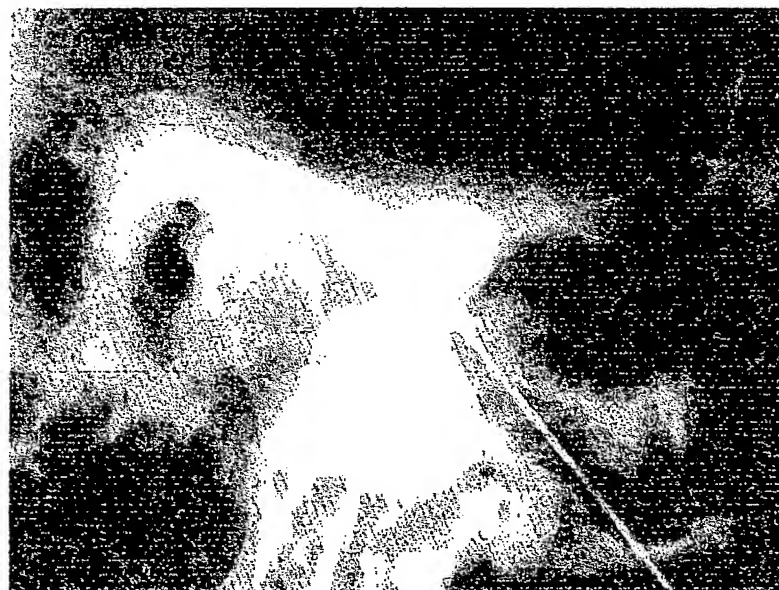


Fig. 2. Metrizamide filling the trigeminal cistern in a lateral view of the skull.

ures.

patients

following the procedure. The other 10 patients all have satisfactory results, though their follow-up period is still limited (1-9 months). Side-effects of the procedure included two cases of mild motor division weakness in the trigeminal distribution that disappeared within 4 weeks. Seven cases demonstrated mild hypoalgesia to pinprick, and there was one instance of hypoaesthesia and two instances of non-painful paraesthesia, all in the affected distribution of the trigeminal nerve.

DISCUSSION

Hakanson's experience with this procedure encompasses 75 patients with a mean follow-up of 17 months and a pain recurrence rate of 18%.⁶ The longest follow-up with a satisfactory result was 4 years. Four of the patients with recurrent pain required a second injection which relieved their pain. Only one of the 75 patients did not respond at all to the first injection. This patient also failed to respond to a second injection.⁶ Only mild facial hypoalgesia was noted in some patients. There was no case of facial dysaesthesia or anaesthesia dolorosa.

Sweet *et al.*,⁷ also obtained successful pain relief in 24 of 27 patients, though they noted a higher proportion of permanent facial hypoalgesia (7 of 24). Facial dysaesthesia were present in 5 patients with predisposing factors.⁹ Post-traumatic and atypical trigeminal neuralgia were the chief causes of short-term pain relief.

The mechanism of action of glycerol has not as yet been elucidated. It is highly hygroscopic and as a result will cause shrinkage of fibres with subsequent re-expansion as the glycerol is absorbed by the nerve fibres. It probably affects principally unmyelinated and, more importantly, pathologically demyelinated large fibres which would account for its therapeutic effect. Sweet *et al.*,⁷ have demonstrated a selective elimination of those components of the trigeminal compound action potential associated with pain as supportive of this hypothesis.

Glycerol trigeminal rhizolysis is a fairly new technique and its place in the armamentarium of treatments for trigeminal neuralgia must still be established, especially in relation to the production of facial dysaesthesia and long-term recurrence rate.

Its simplicity, however, and its acceptability in terms of patients' comfort have persuaded us to recommend this procedure as a first choice in the therapy for those patients with trigeminal neuralgias who are either unable or unwilling to continue taking medication. Its advantages include: (1) no need for general anaesthesia or deep sedation; (2) no need for exact anatomical accuracy within the trigeminal cistern; (3) no need for patient co-operation; (4) no need for expensive equipment; and (5) reduction of patient discomfort.

Prior therapy by other modalities, such as local alcohol injections, may detract from the effectiveness of this treatment. We therefore recommend that this procedure should be utilized before other invasive modes of therapy.

ADDENDUM

Since the preparation of this paper, a further 10 patients have been treated with a mean follow-up of 1

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satisfactory results, though side-effects of the procedure trigeminal distribution that led hypoalgesia to pinprick, instances of non-painful trigeminal nerve.

of 75 patients with a mean 3%.⁶ The longest follow-up with recurrent pain required of the 75 patients did not failed to respond to a second patients. There was no case

of 27 patients, though they (7 of 24). Facial dysaesthesia. Post-traumatic and atypical pain relief.

been elucidated. It is highly with subsequent re-expansion probably affects principally myelinated large fibres which have demonstrated a selective sound action potential asso-

technique and its place in the must still be established, and long-term recurrence

is of patients' comfort have place in the therapy for those able or unwilling to continue: general anaesthesia or deep in the trigeminal cistern; (3) expensive equipment; and (5)

alcohol injections, may detract commend that this procedure

ADDENDUM

Since the preparation of this paper the present series has been expanded to 36 patients with a mean follow-up of 11 months and a success rate of 92%.

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1. AU Wang A.; Jankovic J.
CS Dr. J. Jankovic, Movement Disorders Clinic, Department of Neurology,
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Refs: 96

2. U Borodic G.E.; Acquadro M.A.
CS Dr. G.E. Borodic, 100 Charles River Plaza, Boston, MA 02114, United
States. borodic@aol.com
SO **Journal of Pain**, (2002) 3/1 (21-27).
Refs: 27

3. TI Headache management in an interventional pain practice.
AU Trescot A.M.
CS Dr. A.M. Trescot, 1895 Kingsley Ave., Orange Park, FL 32073, United States
SO **Pain Physician**, (2000) 3/2 (197-200).
Refs: 11

4. TI HEMIFACIAL SPASM - A REVIEW
AU WILKINS R H (Reprint)
CS DUKE UNIV, MED CTR, DIV NEUROSURG, DURHAM, NC 27710
CYA USA
SO **SURGICAL NEUROLOGY**, (1991) Vol. 36, No. 4, pp. 251-277.

5. U Borodic G E (Reprint); Acquadro M A
CS 100 Charles River Plaza, 3rd Floor, Boston, MA 02114 USA (Reprint);
Harvard Univ, Massachusetts Gen Hosp, Sch Med, Dept Anesthesia & Crit
Care, Boston, MA USA; Harvard Univ, Massachusetts Eye & Ear Infirm, Sch
Med, Dept Ophthalmol, Boston, MA USA
CYA USA
SO **JOURNAL OF PAIN**, (FEB 2002) Vol. 3, No. 1, pp. 21-27.

6. TI Use of botulinum toxin to alleviate facial
pain.
AU Girdler N M
SO **BRITISH JOURNAL OF HOSPITAL MEDICINE**, (1994 Oct 5-18) 52 (7) 363.
Journal code: 0171545. ISSN: 0007-1064.

ABSTRACT: Hemifacial spasm (HFS) is a peripherally induced movement disorder characterized by involuntary, unilateral, intermittent, irregular, tonic or clonic contractions of muscles innervated by the ipsilateral facial nerve. We reviewed the clinical features and response to different treatments in 158 patients (61% women) with HFS evaluated at our Movement Disorders Clinic. The mean age at onset was 48.5 ± 14.1 years (range: 15–87) and the mean duration of symptoms was 11.4 ± 8.5 (range: 0.5–53) years. The left side was affected in 56% instances; 5 patients had bilateral HFS. The lower lid was the most common site of the initial involvement followed by cheek and perioral region. Involuntary eye closure which interfered with vision and social embarrassment were the most common complaints. HFS was associated with trigeminal neuralgia in 5.1% of the cases and 5.7% had prior history of Bell's palsy. Although vascular abnormalities, facial nerve injury, and intracranial tumor were responsible for symptoms in some patients, most patients had no apparent etiology. Botulinum toxin type A (BTX-A) injections, used in 110 patients, provided marked to moderate improvement in 95% of patients. Seven of the 25 (28%) patients who had microvascular decompression reported permanent complications and the HFS recurred in 5 (20%). Although occasionally troublesome, HFS is generally a benign disorder that can be treated effectively with either BTX-A or microvascular decompression.

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HEMIFACIAL SPASM: CLINICAL FINDINGS AND TREATMENT

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Hemifacial spasm (HFS) is characterized by initially progressive, involuntary, irregular, clonic or tonic movements of muscles innervated by the seventh (facial) cranial nerve on one side of the face. HFS often initially involves the orbicularis oculi muscle, followed by gradual spread to other parts of the face. Rare cases of bilateral HFS have been reported.^{26,37,68,85,95} Usually without any identifiable etiology, this peripheral movement disorder has been most frequently attributed to compression of the facial nerve at the root exit zone (REZ) by an ectopic anatomical or pathological structure resulting in "ephaptic transmission."^{8,73,74,88} Antidromic stimulation of the facial nucleus has been thought to produce a "kin-

dling" effect.^{65,66} Compression by an atherosclerotic, aberrant, or ectatic intracranial artery near the REZ, first described in 1947 by Campbell and Keedy,¹⁴ has been recognized as one of the most common mechanisms of this condition. Other sources of compression include arteriovenous malformation (AVM),⁷¹ aneurysm,^{71,72} different types of brain tumors,^{13,17,72,93} meningioma,^{16,72,83} and bony abnormalities of the skull^{25,93} localized in the ipsilateral cerebellopontine angle (CPA) or on the contralateral side, distorting the normal anatomy of the ipsilateral facial nerve.^{60,75} Peripheral facial nerve injury or prior Bell's palsy can also result in HFS.^{54,58} At least four families with HFS have been described, suggesting that some patients are genetically predisposed to develop this peripherally induced movement disorder.^{15,18,31,64}

HFS is frequently confused with other facial movement disorders, such as blepharospasm, and other forms of cranial dystonia (CD),^{21,34,38,96} facial tics, myokymia, hemimasticatory spasm, and aberrant regeneration with synkinesis after Bell's palsy.^{21,96} When HFS coexists with trigeminal neuralgia, suggesting that both facial and trigeminal nerves are compromised, it is referred to as "tic convulsif."^{20,36,61}

Abbreviations: AVM, arteriovenous malformation; BL, blepharospasm; BTX-A, botulinum toxin type A; CD, cranial dystonia; CPA, cerebellopontine angle; CT, computed tomography; EMG, electromyography; HFS, hemifacial spasm; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; OMD, oromandibular dystonia; PICA, posterior inferior cerebellar artery; REZ, root exit zone

Key words: hemifacial spasm; botulinum toxin; microvascular decompression; dystonia; blepharospasm

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Previous reports of HFS were published prior to the advent of clinical use of botulinum toxin type A (BTX-A) injections, which has revolutionized the treatment of HFS. In this study we describe the clinical features in a large series of patients studied in a Movement Disorders Clinic and review our experience with BTX-A.

PATIENTS AND METHODS

One hundred and fifty-eight patients with the diagnosis of HFS were evaluated at the Baylor College of Medicine Movement Disorders Clinic during the period 1981–1997. Medical records of all patients with the diagnosis of HFS in our database were carefully reviewed. In addition to a detailed review of the medical records, questionnaires requesting information regarding demographics, race, worsening or alleviating factors, symptoms during sleep, and response to different medicines, BTX-A injections (BOTOX®-Allergan) or surgeries, were mailed to each patient. The clinical data were verified either by a questionnaire or by a telephone interview in 102; 53 patients were unavailable for additional follow-up, and 3 were deceased. Based on the close correlation between the information in the medical records and the data obtained from the telephone interview we used the entire series of 158 patients for the analysis of the clinical features of HFS.

To be included in this study, the patients had to satisfy the following inclusion criterion: unilateral involuntary facial muscle contractions affecting one or more muscle groups innervated by the facial nerve. Patients with bilateral HFS were included if the onset of the facial spasm was not simultaneous and if the contractions were asynchronous. Patients with myokymia (focal undulating muscle contraction), tardive dyskinesia, and other forms of facial or oromandibular dystonic movements were excluded.

Since HFS is often confused with blepharospasm (BL) and CD, we compared our group of patients with HFS with a total of 95 consecutive patients seen in our clinic during the same period, 54 with isolated BL and 41 with primary CD affecting both upper and lower parts of the face. The demographic data, including the age, age at onset, gender, and race, of the three groups of patients were analyzed and compared.

The response to the previous BTX-A injection was evaluated at each follow-up visit. The number of units of the BTX-A, the average frequency of injections, latency from the time of injection to the onset of effect, and the total duration of the effect were recorded for each patient. The peak effect of the injection was assessed according to the following 0–4

scale⁴⁸: 0 = no effect; 1 = mild effect, no functional improvement; 2 = moderate improvement, no change in functional disability; 3 = moderate improvement in both severity and function; 4 = marked improvement in both severity and function. The patients who were only seen once and in whom we were not able to obtain follow-up assessments were excluded from the analysis of response to BTX-A treatment. The side effects of BTX-A injections were also recorded at each follow-up visit.

RESULTS

Among the 158 patients with HFS included in this study, there were 97 (61%) women. The patients were followed for a mean of 17.7 ± 24.4 months (range: 0–112). The mean age was 59.95 ± 14.1 years (range: 29–89), the mean age at onset was 48.5 ± 14.2 years (range: 15–87), and the mean duration of symptoms before diagnosis was 11.4 ± 8.5 years (range: 0–53). This was significantly younger than in patients with BL [56.4 ± 11.5 years (range: 26–77) ($P < 0.0005$)] and was similar to patients with CD [48.7 ± 11.4 years (range: 22–72)]. Similar to the demographic distribution of the BL and CD clinic population, 99 (63%) of our patients with HFS were Caucasians, 21 (13%) Hispanics, 3 (2%) African Americans, and 9 (6%) Asians. In the remaining 26 (16%) the race was mixed or patients either failed to provide adequate information or simply refused to answer questions about racial origin.

Contractions involving the periorcular muscles were present at the onset in 142 (90%) of all patients, with the lower eyelid being affected slightly more often than the upper eyelid; 16 (10%) patients reported initial involvement in other parts of the face (Table 1). The involuntary movement later spread to other parts of the ipsilateral face, affecting other muscle groups innervated by the facial nerve. The orbicularis oculi muscle was most commonly in-

Table 1. Symptom location and anatomic distribution in HFS.

Location	Site of onset by history [n (%)]	Affected site by examination [n (%)]
Frontalis	0 (0)	38 (24)
Orbicularis oculi	142 (90)	152 (94)
Eyebrow	4 (3)	8 (5)
Zygomatic	0 (0)	87 (55)
Cheek	18 (11)	8 (5)
Paranasal	2 (1)	34 (22)
Perioral	15 (9)	99 (63)
Chin/mentalis	0 (0)	33 (21)
Platysma	0 (0)	48 (33)
Other	2 (1)	5 (2)

volved during the course of the condition (150 patients or 94%), followed by the orbicularis oris muscle and the zygomatic muscles. The involvement of the frontalis, corrugator, paranasal region, mentalis, submental area, and the platysma was less common. In some cases, HFS also extended to the periauricular region. Tongue discomfort was reported in 5 cases. Eight patients developed obvious ipsilateral facial hypertrophy.

The symptoms were frequently exacerbated by stress, anxiety, nervousness, and fatigue (Table 2). Voluntary facial movements, particularly pursing of the lips, tended to intensify the facial spasms. Relaxation and alcohol intake were identified as the only two important alleviating factors. With the exception of stress and fatigue, there were no other factors that reliably alleviated or worsened the symptoms. Of the 74 patients who responded to the question whether the facial movements persisted during sleep, 51 (80%) responded affirmatively.

Patients with HFS frequently complain of associated symptoms. Interference with vision, reported by 61 (39%), frequently caused difficulty with reading and driving. The most common complaint was social embarrassment, reported by 65 patients (41%). HFS rarely caused pain unless associated with trigeminal neuralgia, but some discomfort or pain was reported by 17 (11%) patients. Thirteen (8%) had dysarthria secondary to the involuntary facial movements while 6 (4%) reported sialorrhea. Ten (6%) patients reported some degree of facial paresthesia, 7 (4%) had bruxism, and 5 (3%) developed trismus. Twenty (13%) patients reported unilateral or bilateral hearing loss, which did not necessarily correlate with side or severity of the HFS. Only 1 (0.6%) patient reported transient loss of hearing ipsilateral to and

during the active spasm of the facial muscles; 6 (4%) patients described a "clicking" or a "ticking" sound on the same side of the HFS. In some cases, the "clicking" sound was simultaneous and synchronous with the facial muscle contractions. Other complaints included eye irritation ($n = 7$), tearing ($n = 10$), and photophobia ($n = 4$). The neurological examination was usually unremarkable, except for the twitching, but some patients demonstrated subtle unilateral weakness, ipsilateral facial muscle hypertrophy, or both. These changes were, however, difficult to quantitate.

HFS is sometimes associated with other neurological or movement disorders, but the coexistence seems to be coincidental. Eight patients had ipsilateral trigeminal neuralgia and 9 had previous history of Bell's palsy on the same side, with or without residual facial weakness. Among the 5 who had a clear history of previous injuries or trauma on the same side of the face, 4 suffered motor vehicle accidents resulting in skull and cervical fractures ($n = 1$) and facial lacerations ($n = 3$), 6 months to 4 years prior to the onset of their HFS. Probably less relevant disorders that immediately preceded or were coexistent with HFS included: facial "shingles" (3), facial nerve block for dental procedure (1), drainage of gingival abscess (1), and ipsilateral parotid gland surgery (1). Two patients were thought to have psychogenic HFS because of marked distractibility (1) and a response to placebo (1). Although 7 patients had a history of facial cosmetic surgeries, the onset of HFS did not seem to have a direct relationship to the procedures. Only 3 patients reported the presence of similar facial movements in their family members.

Diagnostic studies were generally not helpful in finding the cause of HFS. Twenty-seven (30%) of the 96 who had magnetic resonance imaging (MRI) of the brain had some abnormal finding. Among patients who had abnormal imaging studies, MRI, magnetic resonance angiography (MRA), or contrast angiography, 19 (12%) had vascular abnormalities. These included 10 (6%) with abnormalities of the vertebral basilar system, 2 with tortuous, ectatic basilar arteries, 1 with a basilar aneurysm, 1 with minimal tortuosity of the posterior inferior cerebellar artery (PICA), and 1 with a right frontal and parietal AVM. There were 5 additional cases with nonspecific aberrant or ectatic arteries or tortuosities. Ten patients showed ischemic changes in their imaging tests, but only 3 had pontine involvement; 2 had lesions in the mid pons and 1 had contralateral pontine infarction. Imaging studies also identified one venous angioma in the ipsilateral parietal lobe and one intraventricular papilloma. Surgical removal of

Table 2. Factors modifying symptoms in 158 patients with HFS.

	Worsens	Improves	Unknown or no effect
Stress/anxiety	103	0	55
Fatigue	72	0	86
Exercise	12	10	136
Relaxation	5	47	106
Facial movements	62	6	90
Light	43	2	113
Reading	47	1	110
Talking	53	1	104
Chewing	34	4	120
Driving	26	5	127
Alcohol	6	11	141
Touching the area	7	29	122
Eye movement	32	2	124

the papilloma, found 12 years after the onset of the HFS, did not modify the severity of the HFS. One patient with ipsilateral CPA neurinoma also reported facial pain in the trigeminal distribution associated with marked bruxism. Among the 8 (5.1%) patients who had associated trigeminal neuralgia, 4 had abnormal imaging studies: 3 were found to have unusually tortuous and ectatic basilar arteries and 1 had a CPA neurinoma.

Facial electromyography (EMG), performed in 25 patients, showed in addition to the abnormal facial muscle contractions, evidence of prior facial nerve damage in 7 (28%). Among 9 who had a history of Bell's palsy, the EMG revealed synkinesis in 3. Two additional patients who had no prior history of Bell's palsy also had an abnormal EMG suggesting old facial nerve damage and subsequent regeneration. Other laboratory studies such as the electroencephalogram and brain stem auditory evoked potentials added no useful information.

Most patients received oral medications, BTX injections, surgery, or some combination of these approaches. One hundred and thirty-one (83%) patients tried some medications during the course of their disease, but only 14 (11%) still continue with medical treatment. A total of 6 patients never tried BTX-A injections. Six (5%) patients are receiving combination treatment of oral medications and BTX-A. Carbamazepine was the most popular medication prescribed for HFS, followed by clonazepam, baclofen, other benzodiazepines, anticonvulsants, and anticholinergic drugs. Other miscellaneous medications were also used such as haloperidol, alprazolam, amitriptyline, doxepin, and cyclobenzaprine, but none provided satisfactory or sustained improvement of the involuntary facial movements.

BTX-A injections were used in 110 of 158 patients (70%) during the course of their HFS; among them, 70 (64%) continue this treatment in our clinic and 28 (18%) have been lost to follow-up. Eighty-four (76%) of the 110 patients have had adequate follow-up assessments. The mean total number of BTX-A visits was 5.5 ± 4.4 (range: 1-28) and the mean interval interval was 5.6 ± 1.7 years (range: 3-13). The amount of BTX-A used in each injection varied from 5 to 100 U, with an average of 32.7 ± 12.9 U. The latency from injection to the onset of benefit was 5.4 ± 7.8 days (range: 0-45) and the total duration of benefit averaged 18.4 ± 6.1 weeks (range: 0-37). Sixty-seven (80%) of the 84 patients had a peak effect of 4 (marked improvement in severity and function) and 13 (15%) had a score of 3 (moderate improvement in severity and function). Only 2 patients (1%) reported no improvement with the first injection

and did not return for a follow-up treatment. A total of 59 patients noted at least one side effect following at least one injection; these side effects were rated as mild and were never disabling. They included facial weakness ($n = 25$), lid weakness ($n = 22$), ptosis ($n = 17$), teary or dry eyes ($n = 10$), diplopia ($n = 7$), hematoma ($n = 6$), and diverse other side effects ($n = 5$).

Twenty-eight of the 158 (17%) patients were treated surgically; 25 had microvascular decompression surgery, 1 required clipping of the ipsilateral internal carotid aneurysm, 1 had sinus drainage, and another had orbital myectomy with a complete remission. Thirteen (46%) of the 28 never had BTX-A injections and 9 (8%) had surgical intervention after trying BTX-A injections. Six (21%), including 5 with microvascular decompression and 1 with aneurysm clipping, had recurrence of their HFS and required BTX-A treatment after surgery. Seven (28%) of the 25 who had microvascular decompression reported permanent complications consisting of ipsilateral facial weakness ($n = 4$), hearing loss ($n = 1$), vocal cord palsy ($n = 1$), and dysphagia ($n = 1$).

DISCUSSION

Demographics and Clinical Presentation. This report describes the largest series of patients with HFS since the advent of BTX-A. Similar to CD, HFS seems to be slightly more prevalent in females than males, a finding consistent with previous reports.^{21,27,38,55,87,96} HFS begins on the average 7 years before the age at onset for BL ($P < 0.0005$). There were only 5 (3%) patients in our series with bilateral HFS. In these patients the muscle contractions on the two sides of the face began at different times, and they were asynchronous and asymmetric. Elni and Woltman reported 6 cases of bilateral HFS among 106 patients (5%) in their 1945 study,²⁶ and 40 years later Moller and Moller⁶⁸ described 1 case (0.6%) of bilateral HFS among 143 patients.

Eighty percent of our patients have claimed that their HFS persists during sleep. One polysomnographic study showed persistent, although diminished involuntary facial contractions, during sleep.⁷⁰ Some patients with HFS also report hearing a rhythmic "clicking" sound in the ipsilateral ear, attributed to contractions of the tensor tympani or stapedius muscles.^{6,41} Persistence during sleep and clicking are also characteristic features of rhythmic palatal myoclonus, but this disorder is either idiopathic (essential) or associated with brain stem pathology.

Etiology and Pathogenesis. A number of studies have suggested that the most frequent etiology of

HFS is compression of the facial nerve at its REZ by aberrant or ectatic blood vessels.^{14,58,67} The anterior inferior cerebellar artery or PICA are most commonly involved and unusual tortuosity of these vessels has been frequently found during microvascular decompressive procedures; an ectatic vertebral artery, aneurysm of the basilar artery, and AVM are some of the other vascular abnormalities noted in patients with HFS.^{11,14,40,59,72,79,96} In our studies, tortuosity of the vertebral artery was the most common vascular abnormality found by the imaging studies. Different intracranial ipsilateral or contralateral tumors^{60,75} have also been associated with HFS, including meningioma,^{16,72,88} lipoma,^{42,93} epidermoid tumor,^{7,72} neurinoma,⁷² ganglioglioma,¹³ schwannoma,⁵³ venous angioma,¹⁷ and acoustic neuroma.⁹⁸ HFS has been seen also with tumors distant from the facial nerve REZ.⁹³ One of our patients had contralateral occipital horn choroid plexus papilloma and another had ipsilateral parietal venous angioma. The frequency of mass lesions has been reported in different series to be 0.3–0.5%.^{9,72,93} In our series, 2 of 158 patients (1.3%) were found to have intracranial tumors. Lacunar pontine infarction also has been reported in association with HFS,⁴ and pontine infarction was seen in 3 (1.9%) of our patients, although in 1 case it was located on the side contralateral to the HFS. Bilateral HFS has been reported in association with multiple sclerosis.⁹⁵ Posttraumatic HFS is relatively rare. Besides the 2 cases reviewed by Digre and Corbett in a series of 1688 reported cases,²¹ 4 additional patients were described in 1992.⁵⁸ The facial nerve injury is thought to be the source of ectopic stimuli that generate antidromic transmission and may lead to facial nucleus,^{32,54,58} central, and even cortical, reorganization.⁸⁴ Although stress can increase the symptoms, HFS is rarely of psychogenic origin.⁹¹ Familial cases, suggesting genetic predisposition, are rare, but 3 cases in our series and several in other studies have been described.^{15,18,31,64}

"Tic convulsif" is believed to be caused by compression of both the facial and trigeminal nerves by an abnormal anatomical structure.^{20,36,57,61,76} Microvascular decompression for HFS relieves both conditions.^{11,51,57} Among the 8 patients with "tic convulsif" in our series, 3 had basilar artery abnormalities and 1 had a CPA tumor suggesting more extensive compression. Postparalytic facial synkinesis sometimes follows Bell's palsy^{21,69} and has been attributed to transmission by aberrantly regenerating facial nerve fibers.^{54,69} EMG has been helpful in differentiating this from HFS by documenting electrophysiological evidence of old facial nerve injury and syn-

kinesis.^{28,65} Two of our patients had EMG evidence of synkinesis, suggesting the possibility of prior subclinical facial nerve injury. One patient in our study with recent onset of HFS had a 19-year history of "crocodile tears" and synchronous involuntary eye closing with voluntary mouth opening which developed months after facial nerve decompression for ipsilateral Bell's palsy. A similar case, reported as the "Martin-Amat syndrome," had an unusual form of facial synkinesis following Bell's palsy, characterized by involuntary eye closure associated with voluntary mouth opening.^{81,82} It is quite possible that more detailed EMG studies would reveal a higher frequency of synkinesis, as reported in other series.⁶

Differential Diagnosis. Differential diagnosis of HFS include BL, oromandibular dystonia (OMD), CD, facial tic, masticatory spasm, facial myokymia, focal seizure, and post-Bell's palsy synkinesis.^{21,34,38,96} In contrast to the unilateral contraction in HFS, BL consists of involuntary, bilateral, relatively symmetrical, synchronous contraction of the eyelids. OMD consists of involuntary, repetitive, patterned, and sustained muscle contractions affecting the lower part of the face, mouth, jaw, tongue, and pharynx.^{34,38} Since the onset in over 90% of cases of HFS is in the upper face, involvement of the lower face as the initial manifestation should suggest either OMD or some specific pathology in or around the brain stem. In contrast to the peripherally induced HFS, OMD and BL are focal dystonias of central origin.⁴⁶ Facial myokymia is a continuous, wavelike, undulating, and flickering movement affecting individual muscle fascicles.^{39,43} The underlying lesion is usually at the dorsolateral mid pontine tegmentum adjacent to the fourth ventricle, involving the post-nuclear portion of the facial nerve, as in brain stem gliomas and multiple sclerosis, or the Guillain-Barré syndrome.⁴³ Facial tics can mimic HFS but the movements are more complex, coordinated, multifocal, frequently alternating between the left and right side, and often associated with phonic tics and other features of Gilles de la Tourette syndrome. Unlike HFS, tics are often preceded by a premonitory sensation and are usually suppressible.^{47,56} Simple partial seizures may involve the facial muscles and may then be confused with HFS. Tonic or clonic facial movements, usually unilateral, occur without alteration of consciousness; when continuous, the disorder is designated *epilepsia partialis continua*.¹⁹ Hemimasticatory spasm is a rare disorder in which painful muscle contractions, frequently associated with hemifacial atrophy, affect the jaw-closing

muscles (masseter) innervated by the trigeminal nerve.¹⁰

Neurodiagnostic studies are rarely helpful in HFS. Computed tomography (CT) scan of the head may show some evidence of anomalous vascular anatomy in up to 83% of the cases of HFS,²² but it is not clear whether these abnormalities are pathogenetically related to the HFS. MRI, MRA, and magnetic resonance tomographic angiography may provide useful information about the vertebral-basilar system and the vascular-parenchymal relationship.^{1,29} In one study, all of 13 patients with HFS had evidence of a vascular structure at the root exit zone of the facial nerve on MRI, but 21% of 140 facial nerves of asymptomatic individuals showed similar findings.⁹⁴ Although a screening imaging study, such as CT or MRI, may not be justified in all cases of HFS, it is prudent to employ these diagnostic studies in all atypical cases, particularly when there are abnormal physical findings, such as loss of corneal reflex, loss of hearing, sensory abnormalities, or facial weakness.

Treatment. Treatments for HFS vary from simple massage and application of a heating pad to BTX-A injections and sophisticated microvascular surgery. Different types of medications including carbamazepine, clonazepam, and baclofen produce variable benefit.^{3,5,89} The newer anticonvulsants, felbamate⁶³ and gabapentine,⁷⁸ may also be useful. The benefit derived from medical therapy, however, is often mild, inconsistent, and rarely sustained; only 8% of our patients reported meaningful benefit from one of these medications. Most studies have found treatment with medications unsatisfactory.^{11,52,90} We therefore recommend medications only in very mild cases.

Besides microvascular decompression, surgical treatment options include orbital myectomy,³³ facial nerve block with alcohol,⁹² and resection of the facial nerve or its branches. These procedures have been generally abandoned because of high complication and recurrence rates.⁸⁶ One recent study showed success with extracranial transtympanic needling of the facial nerve with no recurrence after 7 years of follow-up.⁷⁷ Most surgical procedures used today, popularized by Janetta,^{44,45} involve microvascular decompression. This procedure, reported to be successful in 90% of the cases in different series,^{11,12,40,41,79} was the treatment of choice for HFS before the advent of BTX-A injections.^{11,41,72} However, it carries a relatively high, and to many patients unacceptable, risk of complications such as ipsilateral hearing loss (1.6–15%), facial weakness (0.3–

4.8%), hydrocephalus (0.3%), intracranial hematoma (0.7–0.8%), stroke (0.5–0.7%), and even death (0.1–0.7%).^{9,11,35,40,41,51} The reported recurrence rate after surgery varies from 1.1 to 55.5%^{41,51,53,86}; we observed 20% recurrence rate in 25 of our patients treated with this procedure. Reoperation has an even lower success rate and a higher possibility of complications.¹¹

Since the advent of BTX-A, the treatment recommendations have gradually shifted from surgery to chemodenervation.^{2,24,30,50} Some patients report immediate improvement after the injection,³⁰ but the average latency is 5 days.⁵⁵ The average duration of improvement following BTX-A was slightly over 4 months, consistent with the 12–20-week benefit duration reported in other series.^{24,27,30,55,78,87} The average dose used in each treatment visit was 32.7 (range: 5–100) U, similar to that in other series.^{2,24,30,50,52,80,87} Although we have never observed sustained spontaneous resolution, remission from 1 to 9 years has been seen in 4% in one series after 1–6 injections.⁶² It is possible, however, that some of our patients lost to follow-up (18%) achieved spontaneous remission. Similar to other reported results, we demonstrated that 95% of patients had marked to moderate improvement with BTX-A treatment. Ptosis is the most commonly reported side effect from BTX injections and has been observed in 8–37% of the patients.^{2,30,50,52,80,87} In our own experience, temporary facial weakness is the most common (23%) complication, followed by lid weakness (20%) and ptosis (15%). In most cases, however, adjustment of dosage and the site of injection alleviates or prevents such complications after subsequent injection. Distant side effects such as nausea, general malaise or weakness, allergic reactions, or development of antibodies to botulinum toxin have been reported,^{23,49} but the frequency of such complications is low. We have never observed immunoresistance in any of our patients with HFS treated with repeat BTX-A injections during the past 15 years. All the side effects are transient, reversible, and rarely disabling. As techniques of injection improve, it is likely that even the small rate of complications will improve.

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Headach and Facial Pain R sponive to Botulinum T xin: An Unusual Presentation of Blepharospasm

Sharon J. Johnstone, MD, Charles H. Adler, MD, PhD

The diagnosis of blepharospasm is rarely considered in patients complaining of face pain or headache. This patient illustrates the importance of looking for blepharospasm in patients who present with headache or face pain, as her pain and blepharospasm were successfully treated with botulinum toxin type A injections.

Key words: blepharospasm, facial pain, headache, botulinum toxin

Abbreviations: BTX-A botulinum toxin type A

(*Headache* 1998;39:366-368)

Blepharospasm is a focal dystonia of the orbicularis oculi (the corrugator, procerus, and frontalis muscles may also be involved)¹ characterized by repetitive, sustained, involuntary eye closure that can be intermittent or constant. Severity can range from imperceptible to incapacitating functional blindness² restricting a patient's ability to drive, read, and perform activities of daily living.² Blepharospasm may be idiopathic, associated with neurologic diseases,^{3,7} or may be triggered by certain ophthalmologic conditions^{4,8,9} necessitating careful ophthalmologic examination. Eye pain or dry eyes are often associated with blepharospasm,^{10,11} but headache or facial pain is not.¹² We present a patient with blepharospasm who presented with severe headaches and periorbital pain that responded to botulinum toxin type A (BTX-A) treatment.

CASE HISTORY

An 87-year-old woman presented with severe headaches of 1-year's duration, increasing in frequency over several months. She had daily headaches characterized as bilateral, frontal, and

periorbital aching pain in a distribution "as though I am wearing glasses." These headaches were associated with photophobia, but not with phonophobia or nausea, and were improved with recumbency. She denied surface eye irritation, excessive tearing, scleral injection, history of iritis, diplopia, or new visual loss. She denied difficulty with driving, reading, writing, or watching television. Past eye history was significant for bilateral extracapsular cataract extraction and posterior intraocular lens placement in 1989 following YAG laser capsulotomy of the left eye (OS). Herpes zoster ophthalmicus 5 years previously resolved without postherpetic neuralgia. Map-dot-fingerprint (MDF) corneal dystrophy and age-related macular degeneration were diagnosed 4 years prior to evaluation. Six months prior to evaluation, she was noted to have persistently elevated intraocular pressure, OS (22 to 27 mm water) and had been prescribed dorzolamide 1/2% XE, 1 drop OS, each night. Past medical history was significant for hypertension and monoclonal gammopathy of unknown significance. There was no family history of headache, dementia, or movement disorders.

The patient was seen by three neurologists, two ophthalmologists, and her primary care physician and had been given a diagnosis of muscle contraction headaches. Evaluation included laboratory testing which revealed a normal complete blood count, blood chemistries, sedimentation rate, vitamin B₁₂, folate, and thyroid profile. A lumbar puncture was completely normal, including the opening pressure of the spinal fluid. The cerebrospinal fluid (CSF) IgG synthesis rate, CSF index, and cytology were normal. A head MRI, with and without gadolinium enhancement, revealed small-vessel ischemic changes consistent with her age and a retention cyst at the base of the right maxillary antrum. An MRA of the brain was normal. A CT scan of the paranasal sinuses also revealed the cyst. Additionally, psychological evaluation demonstrated a mild memory disorder suggestive of early dementia. A

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corneal specialist had diagnosed mild MDF dystrophy which was quiescent, and without surface symptoms. She had failed multiple courses of antidepressant therapy and had no relief of her pain with supratrochlear and supraorbital nerve blocks. Medications included extended-release nifedipine 30 mg daily, hydrocodone 5 mg and acetaminophen 325 mg every 4 hours as required, paroxetine 20 mg per day, dorzolamide 1/2% XE OS nightly, diphenhydramine 25 mg per day, and acetaminophen 2100 mg per day.

Examination.—On examination, the patient kept her head down with her hand covering her eyes. With her hand moved away and her head up, her neuro-ophthalmologic examination revealed a visual acuity of 20/40 both eyes (OU), best corrected; color vision 15/15, OU; Amsler grid hazy with the right eye (OD); palpebral fissures 8 mm OD, 7 mm OS; 60 blinks per minute; with sustained contraction of the orbicularis oculi, frontalis, and corrugator muscles, bilaterally. No lower facial contractions were noted. Palpation of the orbicularis oculi revealed no tenderness or trigger points, ballottement triggered no pain, and the left globe was slightly firmer than the right. Intraocular pressure by applanation was 18 mm OD, 26 mm OS; slit lamp examination revealed mild MDF corneal dystrophy, OU.

The pupils, eye motility, and cranial nerve examination were otherwise normal. Funduscopy revealed mild macular degeneration. General neurologic examination revealed a peripheral sensory neuropathy in the lower extremities and a mild memory deficit. There were no features of Parkinson disease.

Blepharospasm was diagnosed and paroxetine was discontinued. Her narcotic use was limited (40 tablets per year). The patient was treated with BTX-A, 10 U around the orbicularis oculi and 3.75 U to the corrugator muscles, bilaterally. Within 5 days of treatment, her blepharospasm had improved such that she could maintain gaze with a blink rate of 12 to 20 per minute with no tonic eye closures. Mild lid ptosis was present, bilaterally. Most important to the patient, the headaches and periorbital pain totally resolved and her mood drastically improved. Three months after injection, the BTX-A effect had worn off, and the patient noted a return in her headaches and periorbital pain. Examination again revealed continuous blepharospasm with tonic eye closure. Botulinum toxin type A was injected, and she again had complete relief of her symptoms. She has subsequently undergone seven BTX-A treatments, all of which have relieved her pain.

COMMENTS

Blepharospasm is a focal dystonia which may

be isolated or associated with lower facial spasm (Meige syndrome), mandibular spasm (oromandibular dystonia), or part of a segmental or generalized dystonic syndrome. Blepharospasm may be noted in certain extrapyramidal disorders,^{3,5,6} with specific intraparenchymal lesions, or as an unusual complication of medications.^{4,13} When blepharospasm is isolated, potential triggers such as exquisite photophobia or ophthalmologic disorders should be sought.^{8,10} Blepharospasm may be triggered by ocular symptoms of a foreign body sensation, burning, or irritation^{1,10} or may be preceded by conditions such as iritis, (ocular pain and photophobia) corneal ulcers (ocular pain/irritation), keratitis, scleritis, or acute glaucoma.^{8,10,14} In a review of 272 cases of blepharospasm, Elston et al¹⁰ found that 57% had irritation, dryness, grittiness, or photophobia as the presenting symptom of their blepharospasm. Eleven percent of these patients had demonstrable ocular pathology preceding the diagnosis of blepharospasm.

The association of headache or periorbital eye pain in patients with essential blepharospasm has only rarely been reported.^{12,15} Pain associated with dystonia is frequently reported by patients who suffer from torticollis, writer's cramp, and other limb dystonias. The pain is usually aching in quality. It would seem logical that patients with blepharospasm should complain of aching around the eyes or in the face, but it is unusual for blepharospasm to present with the primary complaint of pain. Inquiry of those with established blepharospasm commonly elicits reports of uncomfortable periorbital sensations. We suspect periorbital pain and headache in blepharospasm are underreported. Patients having a primary headache disorder may complain of photophobia, but usually do not demonstrate involuntary blepharospasm. The photo-oculodysnia syndrome is a unique syndrome of "exquisite light hypersensitivity, dry eyes, ocular foreign body sensation, and blepharospasm"¹⁶ that is distinct from simple photophobia.

Our patient specifically denied current surface eye symptoms. Her MDF corneal dystrophy was mild and quiescent, subjectively and objectively. The intraocular hypertension was mild, painless, and not of acute onset. She had no prior history of headache, and did not use narcotics or anti-inflammatory medication daily or frequently to suggest a contributing rebound phenomenon.

The mechanism for the blepharospasm-induced pain in this patient is unclear. However, the temporal pattern of response and recurrence paralleling the eyelid spasms suggests it is likely muscular in origin. Fine and Digre found that some patients with photo-oculodysnia and blepharospasm had relief of both symptoms with cervical

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HEADACHE

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sympathetic ganglion blocks.¹⁵ This would suggest a sympathetically mediated pain. Other types of dystonia, such as torticollis and foot dystonia, have also been associated with pain and respond to BTX-A injections.^{16,17} Whether pain relief is due to the reduction in muscle spasm, or whether sympathetic mechanisms could be involved is unknown.³ Elston et al¹⁰ found up to a 6-month delay from the diagnosis of their patients' ophthalmic condition to the onset of blepharospasm, noting that some patients initially had excessive blinking. This suggests that ocular pathology may result in focal eyelid dystonia, as has been postulated for other types of peripherally induced dystonia.¹⁸ A disorder of the blink reflex has been postulated in blepharospasm.¹⁹ In conditioning blink reflex trials, Tolosa found that patients with blepharospasm demonstrate enhanced recovery of the after-response, unlike normals, suggesting hyperactive brain stem interneuron activity. Failure to suppress after-responses and apparent facilitation suggests either intrinsic brain stem dysfunction or reduced descending basal ganglionic modulation.¹⁹

We suggest that in some cases, as Pita Saloria and Quintana Conte alluded,⁵ persistent trigeminal afferent stimuli, excessively triggering the trigeminal-palpebral reflex, presumably challenges normal interneuron regulation by producing a constant state of activation, overwhelming the interneurons' ability to suppress further activity. Whether by acquired dysregulation or predisposition,¹⁸ blepharospasm is diminished or eliminated with botulinum toxin injections.

Our patient had complete resolution of her periorbital pain within 5 days of BTX-A injections, and stopped complaining of headaches. We can not conclude whether our patient had blepharospasm-induced pain or pain-induced blepharospasm, although stopping the spasms certainly resulted in pain resolution.

We, therefore, stress the need for a detailed examination of patients with headaches and facial pain, to rule out blepharospasm as the primary disorder. Since BTX-A is the treatment of choice for blepharospasm,^{2,14} we recommend its use in relieving the pain in these patients as well.

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3. Grandas F, Esteban A. Eyelid motor abnormalities in progressive supranuclear palsy. *J Neural Transm Suppl.* 1994;42:33-41.
4. Fahn S. Blepharospasm: a form of focal dystonia. *Adv Neurol.* 1988;49:125-133.
5. Aramideh M, Ongerboer de Visser BW, Holstege G, Majoie CB, Speelman JD. Blepharospasm in association with a lower pontine lesion. *Neurology.* 1996;46:476-478.
6. Jankovic J. Etiology and differential diagnosis of blepharospasm and oromandibular dystonia. *Adv Neurol.* 1988;49:103-116.
7. Lee MS, Marsden CD. Movement disorders following lesions of the thalamus or subthalamic region. *Mov Disord.* 1994;9:493-507.
8. Pita Salorio D, Quintana Conte R. Ophthalmologic causes of blepharospasm. *Adv Neurol.* 1988;49:91-102.
9. Nasr AM. Eyelid complications in trachoma: diagnosis and management. *Acta Ophthalmol.* 1991;69:200-204.
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13. Powers JM. Decongestant-induced blepharospasm and orofacial dystonia. *JAMA.* 1982;247:3244-3245.
14. Borodic GE, Cozzolino D. Blepharospasm and its treatment, with emphasis on the use of botulinum toxin. *Plast Reconstr Surg.* 1989;83:546-554.
15. Fine PG, Digre KB. A controlled trial of regional sympatholysis in the treatment of photo-oculodysnia syndrome. *J Neuroophthalmol.* 1995;15:90-94.
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19. Tolosa E, Montserrat L, Bayes A. Blink reflex studies in patients with focal dystonias. *Adv Neurol.* 1988;50:517-524.

STIC-LL

10/1/18

From: STIC-Biotech/ChemLib
Sent: Tuesday, November 18, 2003 12:55 PM
To: STIC-ILL
Subject: FW: In re: 10/040,830 Journal articles

472268

-----Original Message-----

Fr m: Ford, Vanessa
Sent: Tuesday, November 18, 2003 12:47 PM
T : STIC-Biotech/ChemLib
Subject: In re: 10/040,830 Journal articles

12323697

Please supply the following journal articles:

1. AU Wang A.; Jankovic J.
CS Dr. J. Jankovic, Movement Disorders Clinic, Department of Neurology,
Baylor College of Medicine, 6550 Fannin, Houston, TX 77030, United States
SO **Muscle and Nerve**, (1998) 21/12 (1740-1747).
Refs: 96

COLLECTED

2. U Borodic G.E.; Acquadro M.A.
CS Dr. G.E. Borodic, 100 Charles River Plaza, Boston, MA 02114, United
States. borodic@aol.com
SO **Journal of Pain**, (2002) 3/1 (21-27).
Refs: 27

3. TI Headache management in an interventional pain practice.
AU Trescot A.M.
CS Dr. A.M. Trescot, 1895 Kingsley Ave., Orange Park, FL 32073, United States
SO **Pain Physician**, (2000) 3/2 (197-200).
Refs: 11

4. TI HEMIFACIAL SPASM - A REVIEW
AU WILKINS R H (Reprint)
CS DUKE UNIV, MED CTR, DIV NEUROSURG, DURHAM, NC, 27710
CYA USA
SO **SURGICAL NEUROLOGY**, (1991) Vol. 36, No. 4, pp. 251-277.

5. U Borodic G E (Reprint); Acquadro M A
CS 100 Charles River Plaza, 3rd Floor, Boston, MA 02114 USA (Reprint);
Harvard Univ, Massachusetts Gen Hosp, Sch Med, Dept Anesthesia & Crit
Care, Boston, MA USA; Harvard Univ, Massachusetts Eye & Ear Infirm, Sch
Med, Dept Ophthalmol, Boston, MA USA
CYA USA
SO **JOURNAL OF PAIN**, (FEB 2002) Vol. 3, No. 1, pp. 21-27.

6. TI Use of botulinum toxin to alleviate facial
pain.
AU Girdler N M
SO **BRITISH JOURNAL OF HOSPITAL MEDICINE**, (1994 Oct 5-18) 52 (7) 363.
Journal code: 0171545. ISSN: 0007-1064.

Use of botulinum toxin to alleviate facial pain

Sir,
Botulinum toxin, one of the most lethal biological toxins known, has been found to be of therapeutic value in the treatment of various neuromuscular and ophthalmic disorders (Jankovic and Brin, 1991). Its capacity to produce chemical denervation of muscle and temporary paralysis makes it an intriguing option in the management of intractable muscle spasm (Tim and Massey, 1990).

We report an original use of botulinum toxin in the treatment of temporomandibular joint (TMJ) dysfunction, a syndrome which afflicts over 25% of the population at some stage of their life. Chronic dysfunction is characterised by muscle spasms, trismus and meniscal displacement which results in facial pain and limitation of jaw function (Ogus and Toller, 1981). Although the aetiology is multifactorial, the condition is commonly initiated by psychological stress which leads to spasm, particularly in the masseter and lateral pterygoid muscles (Harris et al, 1993). The outcome of standard treatments using jaw exercises, mouth guards, physiotherapy, anti-inflammatory drugs and joint surgery is unpredictable. We hypothesised that injections of botulinum toxin could be used to selectively weaken the affected muscles and alleviate spasm.

A 34-year-old man presented with a 6-year history of facial pain and difficulty in eating which had started following a bereavement and was unresponsive to routine treatment. Examination indicated bilateral acute tenderness over the masseter muscles and restricted jaw opening, with a maximum interincisal distance of 11 mm. There was a limited condylar movement in the TMJs but no radiographic changes.

After obtaining full informed consent, 250 units of botulinum toxin type A (Dysport, Porton Products Limited) dissolved in 1.25 ml saline were injected into each masseter muscle. The patient was instructed to massage the muscles for 20 minutes to maximise dispersion of the toxin.

At review, 10 days later, the patient reported a 'miraculous' alleviation of pain starting 3 days after the treatment. Jaw function had improved, with the interincisal distance increasing to 34 mm. The only side effect was slight bruising at the injection site which lasted 24 hours. After 6 months, the patient's TMJ showed normal function and he was still completely free from pain.

Botulinum toxin appears to have the potential to relieve the muscle spasm and intractable pain associated with TMJ dysfunction. Functional denervation of specific masticatory muscles leads to temporary paralysis but ongoing pain relief. Its use is suggested for

chronic cases that are responsive to standard treatment regimens.

NM Girdler

Lecturer

Department of Oral and Maxillofacial Surgery

United Medical and Dental School

Guy's Hospital

London SE1 9RT

Harris M, Feinmann C, Wise M, Treasure F (1993) Temporomandibular joint and orofacial pain: clinical and medicolegal management problems. *Br Dent J* 174: 129-36

Jankovic J, Brin MF (1991) Therapeutic uses of botulinum toxin. *N Engl J Med* 17: 1186-94

Ogus HD, Toller PA (1981) *Common Disorders of the Temporomandibular Joint*. John Wright & Sons, Bristol: 47-65

Tim R, Massey JM (1990) Botulinum toxin therapy for neurologic disorders. *Postgrad J Med* 91: 327-34

The NHS's winds of change

Sir,
I read Dr Lafferty's editorial on the clinical tutor (Vol. 52(4) 1994, p.133) with obvious interest and agree wholeheartedly that the role and responsibilities of the clinical tutor have developed and expanded rapidly since the NHS reforms were first introduced. I would, however, like to make the following comment.

Behind (or, more commonly, alongside) every good (or bad) clinical tutor stands his/her own personal aide — the postgraduate centre manager — administrator — secretary (what's in a name!). The changes and increase in workload for the clinical tutor have had an even stronger impact on the centre manager and ultimately means an even bigger increase in workload for them too.

If the clinical tutor is the 'candle in the wind', the centre manager is the 'wind-break' who keeps the candle burning! Our predicament needs recognition too! *Andrina D Hardcastle*
Postgraduate Centre Manager
Bassetlaw Hospital and Community Services Trust
Worksop S81 0JN

Sir,
I share Mr Lafferty's view that progress in postgraduate medical education (PGME) makes considerable demands on the clinical tutor. There is indeed no longer any justification for a 'volunteer' consultant to be suddenly nominated by colleagues to apply for the post of clinical tutor. If units are to be effective providers of education, they must have an appropriate human resource strategy to match the strategy of a business providing education. Trusts, therefore, as providers of education, need to take a long-term view and recruit clinicians into training programmes who have the confidence of colleagues that they will develop the necessary managerial and education skills to become clinical tutors.

At the end of a 'term' as clinical tutor, the generic skills acquired would provide the consultant with many attributes

to undertake other roles within the trust, e.g. clinical director. The recommendations of the Committee of Postgraduate Medical Deans will give trusts a greater sense of ownership of the educational responsibilities for doctors. PGME will not be something 'extra', but an integral part of the trust's business.

Being clinical tutor can be a most rewarding part of a consultant's career. Of course, being clinical tutor requires support from colleagues and it is impossible to undertake the tasks, in even a moderately sized district general hospital, in one session. The education and training roles of a clinical tutor are, however, just part of the personnel activities currently undertaken. I feel that as a clinician, a clinical tutor must keep in touch with trainees, through the roles of career development, and not lose them to personnel specialists. Of course this is not the exclusive responsibility of the clinical tutor, and other clinicians play an integral part.

A supportive organisation with the necessary expertise, working alongside the clinical tutor, will meet the challenges of the hurricane of educational change, and Mr Lafferty's candle will not be extinguished: 'How far that little candle throws its beams — so shines a good deed in a naughty world' (*Merchant of Venice* V.1.90).

DJM Williams

Postgraduate Clinical Tutor

Medical Academic Unit

Broomfield Hospital

Chelmsford CM1 5EJ

Car pollution and asthma prevalence

Sir,
Dr Goodman's interesting and readable 'In the public's view' (Vol. 51(10) 1994, p.557) contains some factual errors and lacks a certain logic. A spokesman for the National Asthma Campaign may well have commented to ITN that 9 out of 11 members of the public would like pollution from cars reduced in order to protect people with asthma. That comment was based on a large poll of the public. Neither a spokesman nor the National Asthma Campaign has, however, ever said that pollution is the cause of the increased prevalence of asthma.

What we have repeatedly acknowledged is the scientific evidence that shows that traffic pollution can cause exacerbations of asthma in those who already have the condition. We have very carefully not said that we believe that traffic pollution is the cause of the increased prevalence; instead we have called for much increased research into the reasons for this, which I believe are probably multifactorial and as likely to reflect changes in the domestic environment as in the wider outdoor environment.

Martyn Partridge

Chairman of the Board of Management

National Asthma Campaign

Providence House

Providence Place

London N1 0NT

STIC-ILL

ND

From: STIC-Biotech/ChemLib
Sent: Tuesday, November 18, 2003 1:38 PM
To: STIC-ILL
Subject: FW: In re: 10/040, 830 Journal articles

472314

-----Original Message-----

From: Ford, Vanessa
Sent: Tuesday, November 18, 2003 1:19 PM
To: STIC-Biotech/ChemLib
Subject: In re: 10/040, 830 Journal articles

Please supply the following:

TI FACIAL NERVE PAIN EXCLUDING TIC DOULOUREUX DIAGNOSIS
AND MEDICAL TREATMENT.

AU DALESSIO D J [Reprint author]

CS DEP MED, SCRIPPS CLIN RES FOUND, LA JOLLA, CALIF 92037, USA

SO (1982) pp. P135-144. BRACKMANN, D. E. (ED.). NEUROLOGICAL SURGERY OF THE
EAR AND SKULL BASE. XIX+408P. RAVEN PRESS: NEW YORK, N.Y., USA. ILLUS.

TI Tic douloureux and diabetes mellitus.

AU Collis J S Jr; Wallace T W

SO CLEVELAND CLINIC QUARTERLY, (1968 Jul) 35 (3) 155-7.

Journal code: 0373162. ISSN: 0009-878

TI Trigeminal glycerol rhizolysis in the treatment of tic
douloureux.

AU Rappaport Z.H.; Magora F.

CS Department of Neurosurgery, Hadassah University Hospital, Ein- Kerem,
Jerusalem, Israel

SO European Journal of Anaesthesiology, (1985) 2/1 (53-57).

TI [Trigeminal neuralgia. Possibility of treating the pain with
transcutaneous nerve block].

TRIGEMINUSNEURALGIE. SCHMERZBEKAMPFUNG DURCH TRANSKUTANE NERVENBLOCKADE.

AU Artner F.

CS Ambulat. f. Phys. Medizin u. Rehab., Burgenlandische Gebietskrankenkasse,
A-7001 Eisenstadt, Austria

SO Fortschritte der Medizin, (1986) 104/38 (711-714). English version.

232594

TI Benign chronic orofacial pain. Clinical criteria and therapeutic
approaches.

AU Dworkin S.F.

CS Dep. Oral Med., Univ. Washington SC-63, Seattle, WA 98195, United States

SO Postgraduate Medicine, (1983) 74/3 (239-248).

I Pain relief from peripheral conditioning stimulation in patients
with chronic facial pain.

AU Eriksson M B; Sjolund B H; Sundbarg G

SO JOURNAL OF NEUROSURGERY, (1984 Jul) 61 (1) 149-55.

Journal code: 0253357. ISSN: 0022-3085.

Vanessa L. Ford

Trigeminusneuralgie

Schmerzbekämpfung durch transkutane Nervenblockade

Von F. Artner

Die Trigeminusneuralgie ist anfallsweise mit heftigen Schmerzen verbunden und durch meist morgens oder nachts auftretende Attacken gekennzeichnet. Das Gebiet, das von Schmerzen befallen ist, entspricht dem Funktionsgebiet des Nervus trigeminus. Bei der Untersuchung der Patienten finden wir auch in schmerzfreien Intervallen Druckpunkte (sogenannte Valleix'sche Druckpunkte) des erkrankten Nerven. Anamnestisch geben die Patienten an, daß sie außer den schon erwähnten heftigen Schmerzen, Verspannungen der Muskulatur, blitzartige Zuckungen sowie Parästhesien hatten.

Bemerkenswert erscheint, daß Ausfallserscheinungen, wie wir sie bei einer Neuritis finden, die mit Paresen sowie Schwinden der Reflexe einhergehen, hier vollkommen fehlen. Auslösendes Moment eines Anfalles ist oft ein kalter Luftzug, auch Niesen und Gähnen. Bei den an Trigeminusneuralgie erkrankten Patienten müssen wir folgendes beachten:

liegt ein Tic douloureux oder eine symptomatische Neuralgie vor? Bei dieser letzteren Form kämen als Ursachen Infektionen in Frage, wie Malaria oder Lues, oder aber es liegt eine Intoxikation durch chronischen Alkoholismus vor. Eine Autointoxikation durch Obstipation wäre als Ursache ebenfalls in Erwägung zu ziehen sowie otologische, ophthalmologische (Iritis) und selbst dentogene Prozesse.

Vor der zu beginnenden Therapie müssen wir vorerst die kausalen Faktoren klären. Sind solche vorhanden, sind diese zuerst einer Behandlung zu unterziehen. Bezüglich der medikamentösen Therapie und der Blockaden mittels Anästhetika sei auf spezielle Arbeiten beziehungsweise Lehrbücher hingewiesen.

Dr. med. F. Artner, Ambulat. f. Phys. Medizin u. Rehab., Burgenländische Gebietskrankenkasse (Leiter: Dr. med. F. Artner), A-7001 Eisenstadt.

Zusammenfassung

Wir berichten über eigene Erfahrungen mit der transkutanen Nervenblockade bei Trigeminusneuralgie. In allen zur Behandlung gelangten Fällen konnten wir bisher keinerlei Nebenwirkungen beobachten. Wir können vom physikalisch-therapeutischen Fachgebiet aus die von Jenkner angegebenen positiven Erfolgszahlen voll bestätigen. Nach unseren bisherigen Erfahrungen stellt die transkutane Nervenblockade

bei der Behandlung des Tic douloureux und der symptomatischen Form der Trigeminusneuralgie eine Bereicherung der physikalischen Therapie dar. Aus Sicht der Sozialversicherung hat dies den Vorteil, daß bei fast allen Patienten die medikamentöse Therapie abgesetzt werden konnte.

Schlüsselwörter: Trigeminusneuralgie — transkutane Nervenblockade mit monopolarer positiven Rechteckstrom

Summary: Trigeminal Neuralgia. Possibility of Treating the Pain with Transcutaneous Nerve Block

We report on our experience with nerve block for the treatment of trigeminal neuralgia. In none of the cases treated did we observe any side effects. We can fully confirm the number of successful treatments reported by Jenkner. According to our present experience, transcutaneous nerve block is a useful additional form of physical treatment for tic douloureux and symptomatic trigeminal neuralgia. From the point of view of health insurance costs, this has the advantage of permitting the termination of medical therapy in almost all the patients.

Keywords: Trigeminal neuralgia — transcutaneous nerve block with monophasic positive rectangular impulse current

Nutzung galvanischer Ströme

Analgetische Wirkung an der Anode

Es ist seit Jahrzehnten bekannt, daß galvanische Ströme, wie wir sie von Batterien, Akkumulatoren oder direkt aus dem Stromnetz mittels Umformer erhalten, zur Behandlung von Neuralgien Verwendung finden. Seine analgetisierende Komponente ist gleichsam die Domäne dieser Stromform.

In erster Linie ist es der Pluspol (Anode), der analgetisch wirkt. Die Anode wird daher als differente Elektrode am

Hauptschmerzpunkt des Nerven fixiert. Die Kathode, der negative Pol, die sogenannte indifferente Elektrode, wird auf den Nerv erregend, — ein Grund, weshalb diese Elektrode möglichst gegenüber der Anode anzulegen ist.

Der konstante galvanische Strom übt anodisch eine analgetische Wirkung aus [3, 10, 11]. Diesen konstanten galvanischen Strom können wir durch Unterbrechung in andere Stromformen umwandeln, wie in Dreieck- oder Rechteckform, wobei bemerkt sei, daß gerade der Rechteckstrom von 2 ms Impulsdauer bei der Behandlung der Trigeminusneur-

algie von Bedeutung ist. Wesentlich erscheint es darauf hinzuweisen, daß dieser Rechteckstrom, wie wir ihn durch die Constant-Current-Schaltung erhalten, einen echten Rechteckstrom im Oszillographen darstellt (Abb. 1). Diese Stromform hat für den Patienten keine unangenehmen Nebenwirkungen.

Vor der Entwicklung der transkutanen Nervenblockade behandelten wir in den physikalischen Instituten die Trigeminusneuralgie auf dreierlei Weise:

1. Mittels der Flächengalvanisation. Die differente Elektrode (Pluspol), war ihrer Form nach eine Gesichtsmaskenelektrode nach Bergonie in einer Größe von 150 bis 200 cm². Die indifferente Elektrode (Minuspol) war von gleicher Größe und wurde im Nacken fixiert. Die Stromdosis lag bei 0,3 bis 5 mA. Die Behandlungsdauer war mit 10 bis 20 Minuten bei einer im Durchschnitt dreimal wöchentlichen Behandlung festgesetzt [4, 5, 6].

2. Die sogenannte Punktg galvanisation, bei der wir die differente Elektrode in der Größe von 5 bis 10 cm² an der Nervenaustrittsstelle fixierten. Die negative oder indifferente Elektrode von der Größe 100 bis 200 cm² wurde im Nacken an der Haargrenze angebracht. Die Stromdosis betrug 0,3 bis 2 mA. Die Zeitdauer je Trigeminuspunkt betrug 5 bis 10 Minuten.

3. Die Behandlung mit Bernardschen Strömen [1] erfolgte mittels kleiner, mit einem Handgriff versehener Schalen-elektroden, die im Abstand von 2 bis 3 cm, also dicht nebeneinander, am Verlauf des Nerven aufgesetzt wurden. Als Stromform wurde der D.F. (diphase fixe), ein vollweggleichgerichteter sinusförmiger Wechselstrom Impuls 100/Sekunde verwendet und anschließend der C.P. (module court periode) angewendet. Vermerkt sei, daß die drei genannten Applikationsformen in vielen Fällen nur temporäre Effekte zeigten, die über sechs bis sieben Wochen nicht hinausgingen. Man mußte dann neuerlich mit einer der genannten Therapien beginnen.

Als Elektrodenmaterial wurden früher Zink- oder Bleifolien von 2 mm Dicke verwendet. Diese Elektroden wurden auf einen vorher befeuchteten, achtfach zusammengelegten Frottee- oder Schaumstoff auf die zu behandelnde Stelle angelegt und mittels Binden oder Heftpflaster fixiert. Um eventuelle verätzende Wirkungen durch den Strom

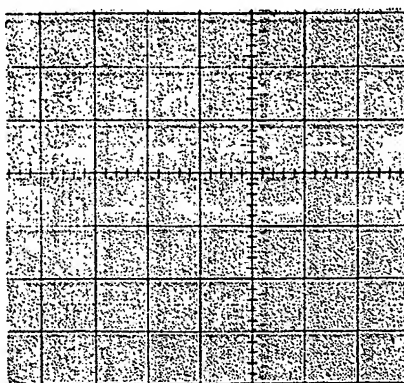


Abb. 1: Monopolarer Rechteckstrom, oszillo-graphische Darstellung.

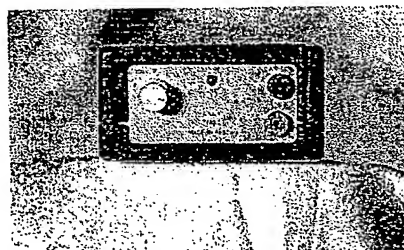


Abb. 2: TNB-I-Einkanalgerät.

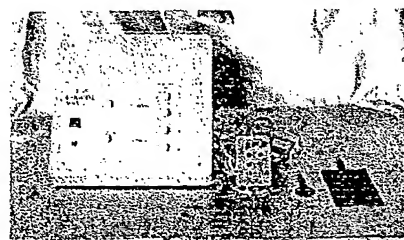


Abb. 3: TNS-IV-4-Kanalgerät.

auszuschließen, mußte der Frotteestoff zirka 2 cm über den Elektrodenrand herausragen. Die modernen Elektroden bestehen aus Kautschuk-Silikon-Material in verschiedenen Größen und Formen und haben den Vorteil wiederholter Verwendbarkeit.

Methodik und Wirkmechanismus

Wahl der Frequenz

Angeregt durch die Literatur [6, 7, 8] einerseits und persönliche Kontakte (F. Jenkner) andererseits haben wir in unserer Ambulanz sowohl einige Transkutane Nervenblockade-I-Geräte (Abb. 2) als auch ein Transkutanes Nervenstimulations-4-Kanal-Gerät (Abb. 3) drei Monate lang getestet. Diese Geräte wurden

uns von der Erzeugerfirma zur Verfügung gestellt.

Zur Frequenz der angewendeten Ströme sowie über die Behandlungsdauer wäre folgendes zu sagen: Die Frequenz, gemessen in Hertz, übt auf die einzelnen Nervenfasern eine differenzierte Wirkung aus, ebenso spielt die Elektroden-größe eine wesentliche Rolle und ihre Anlage über dem Nerv.

Es ist allgemein bekannt, daß Frequenzen von 500 Hertz und höher besonders an Nervenfasern größeren Durchmessers zu einer starken Verkrampfung führen — ein Umstand, der vermieden werden muß. Hingegen bewirken Frequenzen von 50 Hertz und darunter an dünnen, also schmerzleitenden und sympathischen Fasern, unter der Anode eine Hyperpolarisation. Auf diesem Umstand beruht die sogenannte Nervenblockade.

Überlagerung der schmerzlindernden Impulse

Über den Wirkmechanismus elektrischer Reizströme gibt es mehrere Theorien. Diese sind nur teilweise durch exakte Messungen bestätigt, wohl aber therapeutisch gestützt. Im Vordergrund dieser Theorien steht die der Überlagerung der schmerz- und temperaturleitenden Nervenfasern. Da auch hemmende und andere Reflexbahnen den Muskel-tonus beeinflussen, kommt es zu einer Entspannung der Muskulatur. Die damit verbundene Schmerzlinderung wird noch durch Veränderung des Erregungsmusters der Haut- und Schmerzfasern sowie durch eine geringere Freisetzung schmerzzeugender Substanzen (Prostaglandine, Bradykinin, Histamin) der geschädigten Zellen verstärkt. Weiters tritt ein nutritiver Effekt auf, bedingt durch vegetativ gesteuerte Gefäßerweiterung und Beeinflussung der stoffwechselsteuernden Zellorganellen.

Wie Rodiek [11] fand, werden bei der Akupunktur Endorphine freigesetzt. Endorphine sind ein Sammelbegriff für schmerzlindernd wirksame Peptide, die aus Hirnsubstanz und aus der Hypophyse in winzigen Mengen isoliert wurden. Die den Hirn- und Neuropeptiden zugerechneten Endorphine haben teils Hormon-, teils Neurotransmitter-Charakter. Sie wirken wie Enkephaline im Zentralnervensystem analgetisch. Enkephaline sind schmerzlindernd wirksame Oligopeptide und wurden 1975 von Hughes in der Hirnsubstanz entdeckt.

Vermeidung von Hautreizungen

Die angewendete Stromform (positiver Rechteckstrom) von 0,2 ms Dauer und 30 Hertz verhindert infolge der kurzen Impulsdauer unter der Elektrode eine stärkere Rötung und Reizung der Haut.

Genaue Lokalisation der Elektroden

Die Elektroden, die wir bei der transkutanen Nervenblockadebehandlung (Trigeminusneuralgie) verwenden, sind Kautschuk-Silikonelektroden von 10 mm Durchmesser für den Pluspol und 29 mm für den negativen Pol. Die kleinere Elektrode, darauf sei besonders hingewiesen, wird genau im Bereich der Fossa pterigopalatina fixiert, während die größere Elektrode von niedriger Feldstärke an der Nervenaustrittsstelle des Nervus maxillaris, mandibularis oder Nervus supraorbitalis angebracht wird (Abb. 4).

Die SI-Einheit der elektrischen Feldstärke 1 Volt/m ist gleich der Feldstärke eines homogenen elektrischen Feldes, in dem die Potentialdifferenz zwischen zwei Punkten im Abstand 1 m in Richtung des Feldes 1 Volt beträgt. Die elektrische Feldstärke hat die Bedeutung eines Potentialgefälles beziehungsweise die Potentialdifferenz pro Längeneinheit.

Tägliche Behandlung 20 Minuten

Die Behandlung erfolgte täglich während 20 Minuten. Bei unseren meist therapieresistenten Fällen, die bereits mit den verschiedensten Methoden sowohl physikalisch als auch medikamentös behandelt worden waren, sahen wir, daß 20 bis 30 Behandlungssitzungen unbedingt nötig waren. Es gab jedoch auch Patienten, die wir mit weniger Behandlungen wesentlich bessern konnten, so daß sie nach unserer Therapie keine medikamentöse Behandlung benötigten.

Bevor wir auf die Besprechung einzelner Fälle aus unserem Patientengut eingehen, sei hier ausdrücklich festgehalten, daß unsere Patienten von Fachärzten für Neurologie an unsere Ambulanz zugewiesen wurden, um mit der neuen Methode behandelt zu werden, wobei Fälle von Myoarthropathie des Kausystems ausgeschlossen wurden und daher in *Tabelle 1* nicht erscheinen.

Ergebnisse und Kasuistiken**Gesamtansprechrate 76%**

Aus der statistischen Übersicht in *Tabelle 1* geht hervor, daß von insgesamt 53 behandelten Fällen acht mit Tic douloureux und sechs symptomatische Fälle schmerzfrei waren, 15 beziehungsweise zwölf Fälle wesentlich gebessert und nur sieben beziehungsweise fünf, das sind 24%, der Fälle auf diese Therapie nicht ansprachen. Von insgesamt 53 Fällen seien vier Fälle zur Besprechung herausgegriffen.



Abb. 4: Anlage der Elektroden, Trigeminus-II-Ast.

Kasuistiken

Fall 1: Eine 56jährige Patientin leidet seit zwei Jahren an einer linksseitigen Trigeminusneuralgie (Ast II, Typ Tic douloureux laut Befund des überweisenden Facharztes für Neurologie). Subjektiv gibt die Patientin an, kontinuierliche Schmerzen zu haben. Die bisherige Behandlung bestand in einer Neuraltherapie und einer medikamentösen Therapie mit dreimal 200 mg Carbamazepin (in Österreich *Tegretol*; in der Bundesrepublik Deutschland *Tegretal*). Nach Angaben der Patientin war sie nur zeitweise schmerzfrei. In den letzten Monaten nahmen die Schmerzen trotz Carbamazepin vehement zu, so daß die Patientin unsere Ambulanz aufsuchte.

Klinische Untersuchung: Starke Schmerzen auf Druck im Bereich des Valleix'schen Punktes (II). Interner Befund: Pulmo, Cor derzeit ohne Befund. Der Blutdruck war normal, Zähne saniert, Schädelröntgen ohne Befund, Kiefer- und Stirnhöhlen frei. Augen- und otolaryngologischer Befund unauffällig. Nikotin, Alkohol, Venera negiert. Miktion und Stuhl normal.

Wir behandelten die Patientin mit 25 Nervenblockaden täglich über 20 Minu-

ten. Da nach zehn Behandlungen die Schmerzen nachließen, konnten wir die Carbamazepin-Medikation auf zweimal 100 mg herabsetzen. Nach fünf Behandlungen wurde das Medikament vollkommen abgesetzt, nach weiteren zehn Behandlungen konnte die Patientin schmerzfrei entlassen werden. Bei der Nachkontrolle nach sieben Monaten war die Patientin ohne Medikation noch immer schmerzfrei.

Fall 2: Seit 15 Jahren leidet ein 76jähriger Mann laut fachärztlich neurologischem Befund an einer rechtsseitigen Trigeminusneuralgie vom Typ Tic douloureux, subjektiv kontinuierliche Schmerzen aller drei Äste. Bei der bisherigen Behandlung erhielt der Patient über Jahre täglich dreimal 200 mg Carbamazepin, 20 Akupunkturbehandlungen brachten nur zeitweise Schmerzlinderung. Da die Carbamazepin-Medikation vom Patienten nicht mehr vertragen wurde, folgte anschließend eine Behandlung mit Laserstrahlen und Galvanisation, die ihm nur kurzfristig für einige Wochen Schmerzfrieheit brachten.

Klinische Untersuchung: Mittelgroßer Patient, etwas reduzierter allgemeiner Ernährungszustand. Herz dem Alter entsprechend, Blutdruck derzeit 150/95, Pulmo: Emphysem mäßigen Grades. Leber, Milz und Augen ohne pathologischen Befund.

Der Patient wurde 30 Behandlungen mit transkutaner Nervenblockade unterzogen. Schon nach zehn Behandlungen gingen die Schmerzen zurück, die Valleix'schen Punkte waren auf Druck nicht mehr so empfindlich wie bei der Aufnahme. Wir setzten die Carbamazepin-Medikation auf zweimal 100 mg täglich fest. Nach weiteren zehn Behandlungen subjektiv keine Schmerzen, objektiv nur mehr mäßige Druckpunkte im Bereich der drei Trigenimusäste. Dies veranlaßte uns, das Carbamazepin vollkommen abzusetzen. Nach weiteren zehn Behandlungen erzielten wir ohne jegliche Medikation vollkommene Schmerzfrieheit, so daß wir den Patienten nach Abschluß dieser zehn Behandlungen schmerzfrei entlassen konnten. Nachkontrolle nach acht Monaten: weiterhin schmerzfrei ohne Medikamente.

Fall 3: Eine 64jährige Patientin gibt an, seit zehn Jahren an einer linksseitigen Trigeminusneuralgie mit krampfartigen Schmerzen laut fachärztlichem Befund des Neurologen (Ast II und III) zu lei-

den. Bisherige Behandlung: Anfang 1984 Operation nach *Syönquist* im Allgemeinen Krankenhaus Wien, nach dieser Operation ca. zwei Monate vollkommen schmerzfrei. Bald danach stellten sich neuerlich heftige krampfartige Schmerzen ein, daher unterzog sich unsere Patientin neben ihrer Behandlung mit dreimal 100 mg Carbamazepin täglich einer Akupunkturbehandlung. Diese Behandlung brachte ihr durch einige Wochen Schmerzfreiheit. Da sich seit einigen Wochen neuerlich heftige Schmerzen einstellten, erschien die Patientin in unserer Ambulanz:

Klinische Untersuchung: Interner Befund: Herz mäßig links verbreitert, Blutdruck: 155/95. Lunge: mäßiges Emphy-

entlassen. Auch hier erbrachte eine Kontrolle nach fünf Monaten das gleiche Resultat wie bei der Entlassung.

Fall 4: 51jähriger Patient leidet seit zirka acht Jahren an einer beidseitigen Trigeminusneuralgie, krampfartige Schmerzen, rechts mehr als links (Ast II und III laut neurologischem Facharztbefund). Seine bisherige Therapie bestand in galvanischen Behandlungen sowie einer Injektionstherapie und 1981 einer Operation nach *Syönquist*. Postoperativ war er durch ein halbes Jahr vollkommen beschwerdefrei. In den letzten Monaten nahmen seine Schmerzen im Bereich der rechten Gesichtshälfte zu und gingen trotz Medikation von dreimal 200 mg Carbamazepin kaum zurück. Da

ren fünf Behandlungen konnten wir ihn schmerzfrei entlassen. Da der Patient zu einer Nachkontrolle nicht erschien, können wir ihn nur als wesentlich gebessert anführen. Wir haben von den von uns behandelten Fällen vier Fälle herausgegriffen, möchten jedoch darauf hinweisen, daß nicht alle Fälle in der geschilderten Form verliefen.

Bisher konnten wir keine Nebenerscheinungen beobachten. Nach der Behandlung gaben die Patienten lediglich eine leichte Müdigkeit an.

An Kontraindikationen seien erwähnt: Herzschrittmacher sowie schwere pustulöse Akne im Gesicht.

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Anschrift des Verfassers:

Obermedizinalrat Dr. med. Friedrich Artner, Lassallestraße 14/1, A-1020 Wien.

Tabelle 1: Eigene Ergebnisse mit der transkutanen Nervenblockade

	Frei von Schmerzen	Symptomatische Trigeminusneuralgie	%
Fallzahl gesamt	30	23	100
schmerzfrei	8	6	29
wesentlich gebessert	15	12	47
unbeeinflusst	7	5	24

sem; Gebiß saniert, Teilprothese; Schädelröntgen sowie Kiefer- und Nebenhöhlen ohne Befund; Augen ohne Befund. Alkohol, Nikotin negiert, ebenso Venera. Stuhl: zeitweise obstipiert, Miktio normal.

Auf Druck im Bereich des II und III Astes links des Trigeminus heftige Schmerzen, zum Teil Verkrampfung der Gesichtsmuskulatur.

Diese Patientin erhielt 30 transkutane Nervenblockaden und zeigte schon nach zehn Behandlungen tageweise Schmerzfreiheit. Wir reduzierten daher die Medikation auf zweimal 100 mg Carbamazepin täglich.

Nach weiteren zehn Behandlungen setzten wir die Medikation vollkommen ab, da die Patientin angab, fast keine Schmerzen zu haben.

Bei der Zwischenkontrolluntersuchung waren die beiden Äste nur noch schwach druckempfindlich. Da nach weiteren zehn Behandlungen keine Druckpunkte mehr vorhanden waren, wurde die Patientin ohne Medikation schmerzfrei

der Patient die Medikation nicht verweigerte, wurden zehn Akupunkturbehandlungen durchgeführt, auf die sich eine leichte Besserung einstellte. In den letzten drei Wochen heftige Schmerzen rechts, so daß der Patient unsere Ambulanz aufsuchte.

Klinische Untersuchung: Starke schmerzhaftige Druckpunkte des II und III Astes rechts, links keine Druckpunkte feststellbar. Interner Befund: Herz- und Lunge derzeit ohne Befund. Zähne saniert, laut Röntgen keine Herde. Augen, abgesehen von einer leichten Kurzsichtigkeit, ohne Befund; Ohren ohne Befund. Laut Angabe mäßiger Alkoholgenuß, Nikotin täglich zwei bis drei Zigaretten. Venera negiert. Stuhl und Miktio unauffällig.

Wir unterzogen den Patienten einer transkutanen Nervenblockade von 20 Sitzungen und konnten bereits nach fünf Behandlungen eine mäßige Besserung feststellen. Nach weiteren zehn Behandlungen war der Patient ohne Medikation vollkommen schmerzfrei. Nach weite-

From: STIC-Biotech/ChemLib
Sent: Tuesday, November 18, 2003 1:38 PM
To: STIC-ILL
Subject: FW: In re: 10/040, 830 Journal articles

472312

-----Original Message-----

Fr m: Ford, Vanessa
Sent: Tuesday, November 18, 2003 1:19 PM
T : STIC-Biotech/ChemLib
Subject: In re: 10/040, 830 Journal articles

Please supply the following:

TI FACIAL NERVE PAIN EXCLUDING TIC DOULOUREUX DIAGNOSIS
AND MEDICAL TREATMENT.

AU DALESSIO D J [Reprint author]

CS DEP MED, SCRIPPS CLIN RES FOUND, LA JOLLA, CALIF 92037, USA

SO (1982) pp. P135-144. BRACKMANN, D. E. (ED.). NEUROLOGICAL SURGERY OF THE
EAR AND SKULL BASE. XIX+408P. RAVEN PRESS: NEW YORK, N.Y., USA. ILLUS.

TI Tic douloureux and diabetes mellitus.

AU Collis J S Jr; Wallace T W

SO CLEVELAND CLINIC QUARTERLY, (1968 Jul) 35 (3) 155-7.

Journal code: 0373162. ISSN: 0009-878

TI Trigeminal glycerol rhizolysis in the treatment of tic
douloureux.

AU Rappaport Z.H.; Magora F.

CS Department of Neurosurgery, Hadassah University Hospital, Ein- Kerem,
Jerusalem, Israel

SO European Journal of Anaesthesiology, (1985) 2/1 (53-57).

TI [Trigeminal neuralgia. Possibility of treating the pain with
transcutaneous nerve block].

TRIGEMINUSNEURALGIE. SCHMERZBEKAMPFUNG DURCH TRANSKUTANE NERVENBLOCKADE.

AU Artner F.

CS Ambulat. f. Phys. Medizin u. Rehab., Burgenlandische Gebietskrankenkasse,
A-7001 Eisenstadt, Austria

SO Fortschritte der Medizin, (1986) 104/38 (711-714). English version.

TI Benign chronic orofacial pain. Clinical criteria and therapeutic
approaches.

AU Dworkin S.F.

CS Dep. Oral Med., Univ. Washington SC-63, Seattle, WA 98195, United States

SO Postgraduate Medicine, (1983) 74/3 (239-248).

I Pain relief from peripheral conditioning stimulation in patients
with chronic facial pain.

AU Eriksson M.B; Sjolund B H; Sundbarg G

SO JOURNAL OF NEUROSURGERY, (1984 Jul) 61 (1) 149-55.

Journal code: 0253357. ISSN: 0022-3085.

Vanessa L Ford

Pain relief from peripheral conditioning stimulation in patients with chronic facial pain

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GÖRAN SUNDBÄRG, M.D.

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✓ In a prospective study, 50 consecutive patients, referred to a pain treatment unit for surgery to alleviate various forms of facial pain, were all given transcutaneous nerve stimulation (TNS) therapy and followed for 2 years. Of the 44 patients remaining at the 2-year follow-up review, 20 (45%) reported satisfactory analgesia from conventional or acupuncture-like TNS. The latter technique markedly improved the overall results. No serious side effects were seen. Atypical facial pain of known etiology responded best to treatment, but satisfactory relief was often produced with tic douloureux. Duration of the pain condition as well as sex of the patient were predictors of treatment results. It is concluded that TNS therapy represents a valid alternative to surgery when pharmacological therapy fails, especially in the elderly and in patients with atypical facial pain.

KEY WORDS • pain • facial pain • trigeminal nerve • nerve stimulation • transcutaneous nerve stimulation

PATIENTS with chronic so-called intractable facial pain may present management problems. This is true for typical trigeminal neuralgia (tic douloureux) as well as for atypical forms of facial pain.^{1,18,24}

In the treatment of tic douloureux, systemic administration of carbamazepine^{3,5} has for many years replaced alcohol blocks¹³ as the treatment of choice. About 70% of the patients are said to report good or excellent analgesia initially.^{25,32} However, side effects are frequent, often due to overdosage, and long-term follow-up studies have shown that only 25% to 35% of the patients enjoy excellent or good pain relief for more than 5 years as a result of carbamazepine treatment.^{30,32} In a few of the remainder systemically administered phenytoin is effective,¹⁸ but for the others surgical procedures have offered the only chance of relief. The early nonselective techniques carried a significant risk of general as well as local complications.^{23,25} The more selective techniques now used, such as controlled thermocoagulation of the trigeminal ganglion³¹ and retrogasserian glycerol injection,¹² have fewer side effects and can be repeated if necessary.

A different line of therapy has developed from the hypothesis that trigeminal neuralgia is a result of vascular compression of the trigeminal nerve root.⁶ Decompression by microsurgical procedures has been reported successful in 70% to 80% of the patients so treated,^{2,15,33} even if the percentage of cases with signifi-

cant compression found was low (46%).³³ However, as with all surgical procedures, these operations involve potential hazards to the patients as well as a need for trained surgeons and in-patient facilities.

In cases of atypical facial pain,^{10,26} with or without an identifiable organic cause, antiepileptic drugs are generally ineffective. Alcohol injections or surgery, even if giving temporary relief, may later result in a considerable worsening of the condition.^{11,24} Conventional analgesics may be useful when there is an organic cause for the disorder, and tricyclic antidepressant drugs may help when there is not.¹ The available therapeutic methods, however, leave many patients unaided and substantially handicapped by their chronic facial pain.

During the last decade, treatment by conditioning stimulation of peripheral nerves has become increasingly used for patients with acute and chronic pain conditions.^{19,20,34} A long-term follow-up study of the effect of two types of transcutaneous electrical nerve stimulation (TNS) showed that, after 2 years, 31% of patients referred to a neurosurgical department still experienced useful analgesia from daily TNS treatment.⁹ Among these successfully treated patients with chronic pain were several who had previously had intractable facial pain, some of whom had had to use a newly developed TNS technique (acupuncture-like TNS⁸) to obtain pain relief.

Apart from the need for alternative therapeutic meth-

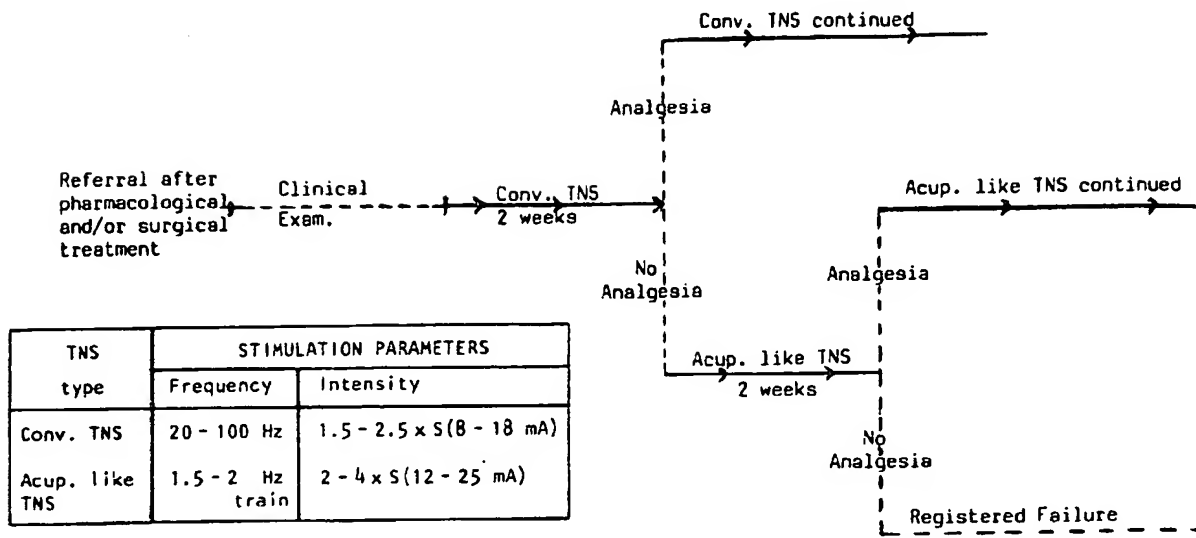


FIG. 1. Scheme illustrating the transcutaneous nerve stimulation (TNS) treatment protocol. Conv = conventional; acup.-like = acupuncture-like; S (sensory threshold) = the current at perception threshold in mA.

ods among patients with intractable facial pain, it seemed of great interest for the evaluation of the TNS techniques to test and follow a group of patients suffering from chronic pain that was less varied as to type and location than in previous studies. We therefore initiated a prospective long-term follow-up study of 50 patients with intractable facial pain, treated with conventional^{14,34} or acupuncture-like^{8,9} TNS. The facial pain conditions treated represent two types of pain; namely, acute intermittent (tic douloureux) and chronic continuous (atypical facial pain). The study and the results obtained are the subjects of this report.

Clinical Material and Methods

Patient Population

The series included 50 consecutive patients with intractable facial pain who were referred to the Department of Neurosurgery at Lund University Hospital for surgery. Twenty-one patients had been classified as having tic douloureux. To comply with the diagnostic criteria, the pain had to be: 1) truly paroxysmal; 2) unilateral; 3) provokable by non-nociceptive facial stimuli; 4) confined to the innervation area of one, two, or three trigeminal branches; and 5) not associated with sensory or other neurological deficit.

There were 11 men and 10 women in the tic douloureux group. Their mean age was 65 years (range 34 to 88 years), and the median duration of pain was 8 years (range 2 to 18 years). All had initially experienced pain relief with carbamazepine. However, diminishing effectiveness of the drug or marked side effects, including allergic reactions, had limited its usefulness or made use impossible. Repeated alcohol injections of one or several distal trigeminal nerve branches had given tem-

porary pain relief to 12 of these 21 patients. Of these 12 patients, seven had also been subjected to surgery (in most cases fractionated heating of the Gasserian ganglion), but the procedures had only given short-term relief. As a result of repeated treatment with injections or surgery, three patients had over the years developed a more continuous aching pain. These three patients and five others had sensory deficits when they entered the present study.

Twenty-nine patients did not fulfill the criteria for tic douloureux and will be considered here as having "atypical facial pain." In 18 of these patients the pain resulted from accidental or surgical trauma (11 patients), cerebrovascular disease (five patients), or herpes zoster ophthalmicus (two patients). In 11 patients no organic cause of the pain could be found. There were 17 men and 12 women in this group; the mean age was 58 years (range 23 to 84 years) and their median duration of pain was 5 years (range 1 to 30 years). All patients but one reported their pain to be almost constantly present, with exacerbations lasting for several hours to days. It was described as deep, dull, aching, or burning. Treatment with carbamazepine, conventional analgesics, antidepressants, or sedatives had not significantly relieved the pain, and 17 patients had been subjected to repeated alcohol injections and/or surgery, in some cases with partial or temporary relief.

Method of Treatment

The treatment with TNS was fully described to the patients, and their consent was obtained. After the initial examination, including sensory testing of the head and neck area, stimulation treatment was tested in an out-patient unit according to the scheme described below and illustrated in Fig. 1. All patients were tested

Conv. TNS

Acup. like

FIG. 2. Acup. like transcutaneous nerve stimulation (black electrode) and the cathode. Low frequency (acup.-like) in text.

in an identical manner as planned.

First, conventional 100-Hz stimulation. The electrode was placed in the second electrode area was in patient pre-electrode.

Each patient was tested and was in minutes. The number of patients who did not respond to TNS at rest was told not to respond and warned of worsened symptoms. However, the lowered intensity was constructed to frequency was the most patient was after 2 months.

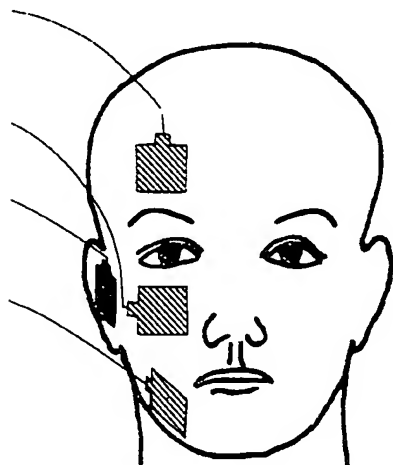


FIG. 2. Upper: Electrode placements for acupuncture-like transcutaneous nerve stimulation (TNS). The anode (black electrode) was located anterior to the external meatus and the cathode (active electrode, hatched) over the center of pain. Lower: Conventional (Conv.) TNS and acupuncture-like (acup.-like) TNS stimulation patterns used as described in text.

in an identical fashion. Later, an individualized regimen was planned.

First, conventional TNS was given with continuous 100-Hz stimulation at an intensity that gave strong paresthesias without being painful³⁴ (Fig. 2). One electrode was usually placed in front of the ear and the second electrode placed according to which trigeminal area was involved. Polarity was chosen according to patient preference. In some patients the most effective electrode position had to be established gradually.

Each patient was given a stimulator for home use and was instructed to apply TNS for a minimum of 30 minutes, three times daily. They were free to increase the number of stimulation sessions if necessary. The patients with tic douloureux were asked to be careful not to stimulate trigger points and were advised to use TNS at regular intervals between attacks. They were told not to expect to be able to control ongoing attacks and warned that stimulation treatment might actually worsen such an attack. If, after a 2-week trial period at home, there was a subjective report of a generally lowered pain level and/or diminishing frequency or intensity of paroxysmal attacks, the patient was instructed to carry on and to vary the stimulation frequency within the 20- to 100-Hz range in order to find the most comfortable frequency for pain relief. The patient was seen again after another 2 weeks, and then after 2 more months.

If, after the first 2-week trial period, there was no significant pain relief, the patient was instructed how to use the stimulator for acupuncture-like TNS. The positive electrode was then placed in front of the ear and the negative electrode over the forehead, cheek, or chin. The stimulator was set for a train (7 pulses at 100 Hz) given at a repetition rate of 1.5 to 2 Hz,^{8,9} and the electrodes adjusted so that visible muscle contractions were produced in the area of pain (Fig. 2). If, after another 2-week trial period at home, there was still no report of significant pain relief, the TNS trial was recorded as a failure. If stimulation treatment was reported to reduce the intensity and frequency of pain paroxysms, or produced useful relief in patients with non-paroxysmal atypical intractable facial pain, the patient was instructed to continue with the treatment and was seen again 2 months later.

If the patients, when seen 3 months after their initial visit, reported useful pain relief and wished to continue TNS treatment, the outcome of therapy was recorded as successful. When patients continued to use small amounts of carbamazepine or other analgesic agents together with stimulation treatment, it was judged as moderately successful. All patients were seen at regular intervals for 2 years or until the treatment was terminated. When pain relief seemed stable or during periods of spontaneous remission, patients were instructed to try to reduce the duration and frequency of the stimulation periods as much as possible.

The stimulator used is a portable constant-current unit that delivers conventional or acupuncture-like TNS by monophasic square-wave pulses of 0.2-msec duration at a maximum of 60 mA into a load of 2500 ohm.* The stimulation was given via standard square carbon rubber electrodes, usually 6 sq cm in size, coated with conductive gel. Stimulation intensity (Fig. 1) was 1.5 to 2.5 times the perception threshold in conventional TNS (usually 8 to 18 mA), and 2 to 4 times the perception threshold in acupuncture-like TNS (usually 12 to 25 mA).

Statistical Assessment

For evaluation of differences between groups the chi-square test was used. If any of the calculated expected numbers for the four fields was 5 or less, Yates' correction was used.

Results

After 3 months of treatment, 16 (32%) of the 50 patients experienced successful or moderately successful pain relief with conventional TNS only (Fig. 3). Of the 34 patients who did not benefit from conventional TNS, acupuncture-like TNS proved to be satisfactory in 13

* Stimulator manufactured by Cefar Medical Products, Lund, Sweden.

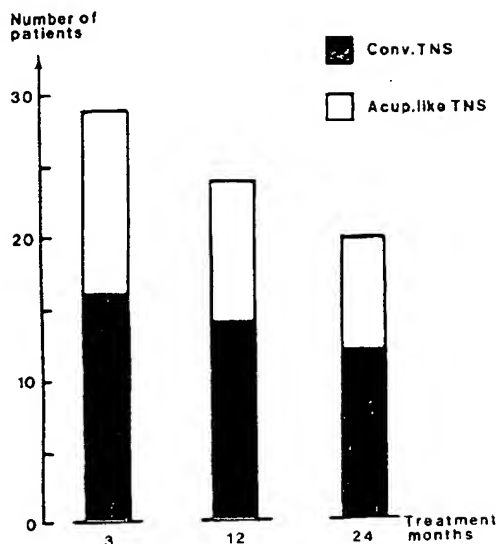


FIG. 3. Numbers of patients experiencing satisfactory pain relief at the times indicated. Black bars indicate results from conventional transcutaneous nerve stimulation (TNS), white bars indicate results from acupuncture-like TNS.

patients. Thus, in all, 29 (58%) of the 50 patients experienced pain relief from TNS. Twenty patients used stimulation only and were considered a success, and nine patients who added small amounts of adjuvant pharmacotherapy were considered a moderate success. Seven patients who had not been working for a long time because of their facial pain went back to work.

At 12 months, two patients had died from unrelated disease and one had a period of spontaneous remission and was not using the stimulator. Of the remaining 47 patients, 24 (51%) were still using TNS and achieving satisfactory pain relief. At 24 months, three patients had a spontaneous remission of their pain and one more had died; 20 (45%) of the remaining patients reported satisfactory analgesia from TNS (Fig. 3).

Treatment results at 3 months were evaluated in relation to the TNS technique used, etiology, and duration of the intractable facial pain condition, sex, main complaint of pain, and results of sensory examination at the time when TNS treatment was started (Table 1). Of the 21 patients with tic douloureux, 11 were in the successful or moderately successful group. Five of these had to use acupuncture-like TNS to achieve satisfactory pain relief (Table 1). Among the patients with atypical facial pain, 11 had pain of unknown etiology; four of these experienced satisfactory relief, two with acupuncture-like TNS. Similarly, among the 18 patients with known etiology of their pain, 14 were in the successfully or moderately successfully treated group, and six of these employed acupuncture-like TNS. There was no significant difference in treatment success between patients with tic douloureux (11 of 21 patients) and atyp-

TABLE 1
Outcome of TNS treatment in relation to clinical data*

Clinical Data	Success	Failure
sex		
male	20 (8)	8
female	9 (5)	13
initial diagnosis		
typical trigeminal neuralgia	11 (5)	10
other forms of intractable facial pain		
unknown etiology	4 (2)	7
known etiology	14 (6)	4
previous treatment		
pharmacological treatment only	13 (5)	8
alcohol blocks or surgery	16 (8)	13
duration of pain (yrs)		
< 6	19 (7)	7
≥ 6	10 (6)	14
main complaint		
pain paroxysms	8 (4)	11
continuous pain	21 (9)	10
cutaneous sensation		
normal	11 (3)	8
hypesthesia or dysesthesia	18 (10)	13

* TNS = transcutaneous nerve stimulation. Numbers in parentheses indicate successful acupuncture-like TNS therapy.

ical facial pain (18 of 29 patients). However, significantly ($0.025 < p < 0.05$) better results were obtained in patients who had atypical facial pain with a known organic cause as compared to all other patient groups (Table 1). The median duration of pain for all patients was 6 years. The success rate of TNS was significantly ($0.025 < p < 0.05$) higher among patients with a pain history of less than 6 years than in the group with a longer history of facial pain (Fig. 4). The mean duration of pain was similar among men (7 years) and women (8 years).

We found a significantly ($0.025 < p < 0.05$) higher number of men than women in the successfully treated group. This is further illustrated in Fig. 5, where it can be seen that with atypical facial pain of unknown and known origins the representation of men and women in relation to success or failure is proportional to their total numbers in the diagnostic groups. On the other hand, among patients with tic douloureux, the representation of men in the successful group was higher than in the unsuccessful group.

There was a nonsignificant tendency for truly paroxysmal facial pain to be more resistant to stimulation treatment (11 of 19 patients) than pain of the more continuous type (10 of 31 patients, Table 1). In an earlier report,⁹ acupuncture-like TNS was noted to be of special value when destructive surgery had been performed with resulting cutaneous hypesthesia or dysesthesia within the area of pain. In the present group of patients with facial pain, the difference between those with normal sensitivity (three of 11 patients) and those with hypesthesia or dysesthesia (10 of 18 patients),

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TNS results

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J. Neurosurg.

Peripheral conditioning stimulation for facial pain

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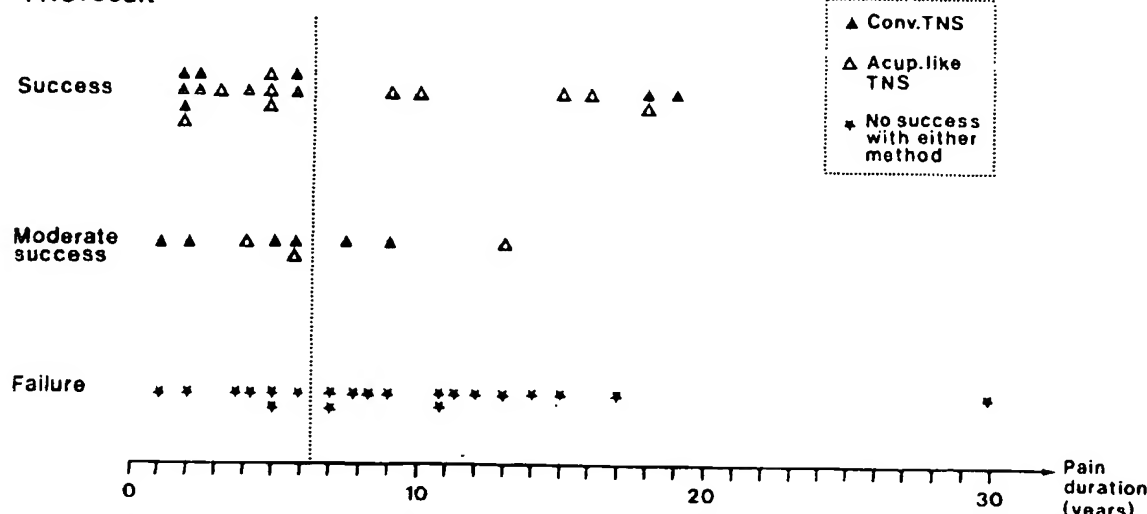


FIG. 4. Results of transcutaneous nerve stimulation (TNS) given in relation to pain duration and TNS technique used. "Success" and "moderate success" are defined in text. Dotted line denotes median pain duration among these patients. Conv. TNS = conventional TNS; acup.-like TNS = acupuncture-like TNS.

as regards method of stimulation, was not significant, however.

Side effects were few. Four patients with typical trigeminal neuralgia reported intensified pain when TNS was used during the actual pain paroxysms. Four patients had marked skin reactions which could be controlled by change of electrodes and tapes. Side effects did not warrant termination of treatment in any of these patients.

Discussion

The present study has confirmed our initial observations⁹ that TNS may be a worthwhile choice of therapy in patients with intractable facial pain. After about 3 months of TNS therapy, about half of the patients with tic douloureux, whose symptoms were often of considerable duration, and two-thirds of those with atypical facial pain achieved satisfactory pain relief.

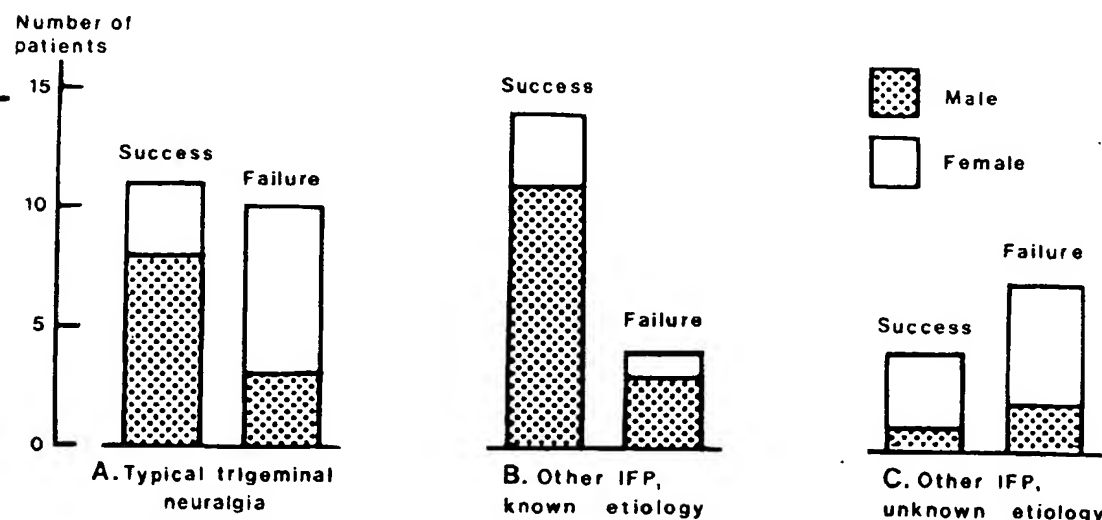


FIG. 5. Results of transcutaneous nerve stimulation in relation to diagnosis of intractable facial pain (IFP) and sex of the patient.

Even after 2 years, 45% of the 44 patients remaining in the study used TNS regularly and experienced satisfactory relief. No serious side effects were seen. All of these patients had severe conditions and were judged to be failures as regards conservative treatment; however, the results of this study show that TNS therapy may well be a relevant alternative to surgical procedures. This may be so for elderly tic douloureux patients, in whom surgical risks are more serious,^{2,15} and for all patients with atypical facial pain, where surgical results are not encouraging.^{10,24}

Interestingly, the newly introduced technique of acupuncture-like TNS⁸ seems to have improved the results considerably as compared to the use of conventional TNS.³⁴ This may well explain why our results with intractable facial pain are superior to those reported by others,^{10,21} but see the report of Ihalaenen and Perkki.¹⁴ The treatment success seen after 2 years in this study (45%) is higher than that reported by us in a previous group of patients consecutively referred for chronic pain to the same pain treatment unit.⁹ One possible explanation for this difference is the relative ease with which coarse nerve bundles in the facial region are stimulated as compared to the technique in many other body areas. Another explanation may be that the pain conditions were well defined and neurogenic,²⁷ and a third suggests that psychogenic factors are less predominant in this group.²²

Among factors predictive for the outcome of TNS, a short duration of the painful condition favors a good result, so did a known precipitating cause among the patients with atypical facial pain. However, the tendency for atypical facial pain to be more amenable to TNS therapy than tic douloureux was not significantly different. Interestingly, men with intractable facial pain, notably those with tic douloureux, enjoyed better treatment results than did women. This might indicate that the men in this sample adjusted better to the occasionally unpleasant stimulation, which could also be considered a social handicap due to the facial electrodes, even if used only 30 to 90 minutes a day. Moreover, psychogenic factors may have been more important among the women.^{22,29}

As regards the possible mechanisms of action of conventional and acupuncture-like TNS, it is interesting that both techniques seem to relieve painful conditions of acute intermittent (tic douloureux) as well as of chronic continuous (atypical facial pain) character. This appears to be true for pain of presumed peripheral as well as of presumed central origin. Thus, successfully treated atypical facial pain was in some instances due to peripheral lesions (herpes zoster neuritis, trauma), in others to cerebrovascular disease. Tic douloureux has been ascribed to peripheral (nerve root compression,⁶ segmental demyelination,¹⁶ exaggerated dorsal root reflexes⁴) as well as to central causes.¹⁷ Taken together, these observations favor a central mechanism of action for TNS. This is in agreement with the observation that

analgesia from acupuncture-like TNS is usually reversible by naloxone,²⁸ indicating an opioid link. However, analgesia from conventional TNS cannot be reversed by naloxone.²⁸ On the other hand, both techniques change sensory thresholds of healthy subjects on both sides after unilateral stimulation, supporting the concept of a central mechanism.⁷

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TI FACIAL NERVE PAIN EXCLUDING TIC DOULOUREUX DIAGNOSIS
AND MEDICAL TREATMENT.

AU DALESSIO D J [Reprint author]

CS DEP MED, SCRIPPS CLIN RES FOUND, LA JOLLA, CALIF 92037, USA

SO (1982) pp. P135-144. BRACKMANN, D. E. (ED.). NEUROLOGICAL SURGERY OF THE
EAR AND SKULL BASE. XIX+408P. RAVEN PRESS: NEW YORK, N.Y., USA. ILLUS.

TI Tic douloureux and diabetes mellitus.

AU Collis J S Jr; Wallace T W

SO CLEVELAND CLINIC QUARTERLY, (1968 Jul) 35 (3) 155-7.

Journal code: 0373162. ISSN: 0009-878

TI Trigeminal glycerol rhizolysis in the treatment of tic
douloureux.

AU Rappaport Z.H.; Magora F.

CS Department of Neurosurgery, Hadassah University Hospital, Ein- Kerem,
Jerusalem, Israel

SO European Journal of Anaesthesiology, (1985) 2/1 (53-57).

TI [Trigeminal neuralgia. Possibility of treating the pain with
transcutaneous nerve block].

TRIGEMINUSNEURALGIE. SCHMERZBEKAMPFUNG DURCH TRANSKUTANE NERVENBLOCKADE.

AU Artner F.

CS Ambulat. f. Phys. Medizin u. Rehab., Burgenlandische Gebietskrankenkasse,
A-7001 Eisenstadt, Austria

SO Fortschritte der Medizin, (1986) 104/38 (711-714). English version.

TI Benign chronic orofacial pain. Clinical criteria and therapeutic
approaches.

AU Dworkin S.F.

CS Dep. Oral Med., Univ. Washington SC-63, Seattle, WA 98195, United States

SO Postgraduate Medicine, (1983) 74/3 (239-248).

I Pain relief from peripheral conditioning stimulation in patients
with chronic facial pain.

AU Eriksson M B; Sjolund B H; Sundbarg G

SO JOURNAL OF NEUROSURGERY, (1984 Jul) 61 (1) 149-55.

Journal c de: 0253357. ISSN: 0022-3085.

Vanessa L. Ford

Benign chronic orofacial pain.

Clinical criteria and therapeutic approaches

Samuel F. Dworkin, DDS, PhD

Preview

Benign orofacial pain stems from many causes—neuropathy, musculoskeletal disorders, even emotional stress. Because of this diversity, diagnosis is difficult, and treatment is often based on the predilection of the physician. Dr Dworkin describes the two principal types of benign chronic orofacial pain—trigeminal neuralgia and TMJ pain-dysfunction syndrome—and the various surgical and pharmacologic therapies used to relieve this often intense and intolerable pain.

Benign orofacial pain syndromes are disorders in which mandibular and maxillofacial pain is the central and often exclusive symptom. These disorders fall into three major categories: (1) pain stemming from neuropathy, especially trigeminal neuralgia, (2) pain stemming from musculoskeletal disorders, especially temporomandibular joint (TMJ) and/or myofascial pain syndromes, and (3) a miscellaneous category of pain syndromes comprising infrequently reported pain states, including referred pain and psychogenic pain.

Classification and differential diagnosis of orofacial pain are complex. The facial structures are of diverse embryologic origin, have an intricate cranial and cervical innervation and blood supply, and contain organs of special sense. Pain in the region may arise from many organs and structures (teeth, periodontium, TMJ, muscles,

ears, eyes, nose, bones, blood vessels), from disease of nerves that innervate the area (especially the fifth, seventh, and ninth cranial nerves and the cervical spinal nerves), or from remote sources such as brain tumor or, rarely, coronary artery disease.

Moreover, the orofacial region has such great psychologic significance regarding appearance and communication that facial pain may be experienced at times of emotional stress, especially during prolonged anxiety and depression. Such pain has been reported in both the presence and the absence of observable pathologic changes.¹ This review describes the two most important and common benign chronic orofacial pain states, trigeminal neuralgia and TMJ pain-dysfunction syndrome.

Trigeminal neuralgia

The most important orofacial neuralgias are varieties of trigeminal neuralgia.

ETIOLOGY AND DIAGNOSIS—

True trigeminal neuralgia (tic douloureux) occurs in a relatively fixed pattern along one or more branches of the trigeminal nerve in middle-aged and elderly persons. Atypical trigeminal neuralgia is a more loosely defined collection of orofacial neuralgias in which distribution of pain and age of onset are variable. Orofacial neuralgias with specific causes include post-traumatic and postherpetic trigeminal neuralgia.

Sweet² has provided the most enduring classification of trigeminal neuralgia: (1) idiopathic (central, true trigeminal neuralgia, or tic douloureux), (2) symptomatic of some other specific neurologic entity (ie, postherpetic, posttraumatic, tumors, multiple sclerosis), sometimes called secondary trigeminal neuralgia, and (3) atypical.

The etiology of primary and atypical trigeminal neuralgia remains largely unknown, but opinion is divided between peripheral and central theories. Peripheral theories are more common and have been favored historically. They ascribe the neuralgia either to compression of the dorsal root by exostoses of the petrous portion of the temporal bone^{2,3} or to compression of the trigeminal nerve in the posterior fossa by vascular

continued

The etiology of primary and atypical trigeminal neuralgia remains largely unknown, but opinion is divided between peripheral and central theories.

loops.^{4,5} A recent controversial theory suggests that chronic periapical infection may be responsible for primary and atypical trigeminal neuralgia.⁶

Advocates of a central etiology point to myelinization disorders, location of trigger points in different divisions from those causing the pain, the frequent absence of a neurologic deficit, and the ability of diverse non-painful stimuli to trigger intense paroxysmal trigeminal pain.⁷ The important finding that the central-acting antiepileptic drug carbamazepine (Tegretol) is effective against trigeminal neuralgia supports a central etiology. Most researchers⁸ remain persuaded that peripheral pathologic processes may trigger primary trigeminal neuralgia but do not cause this orofacial pain syndrome.

The diagnosis of primary trigeminal neuralgia (tic douloureux) is based principally on the criteria of White and Sweet.^{2,9} Classic features are (1) excruciating, lancinating, searing paroxysmal pain lasting seconds to minutes, (2) pain provoked by nonnociceptive stimuli to trigger zones, (3) pain occurring along the anatomic distribution of the fifth cranial nerve, (4) unilateral pain in any one paroxysm, and (5) no objective loss of sensation.

Less classic features, which

distinguish atypical or secondary trigeminal neuralgia from primary trigeminal neuralgia, include continuous or long-lasting burning or aching pain, (2) episodic pain not provoked or worsened by stimulation but spontaneously recurrent, (3) pain extending to the neck and posterior scalp, (4) pain remaining unilateral, and (5) spontaneous hypesthesia unrelated to therapy. Most investigators also report psychologic symptoms, notably depression.

When symptoms of trigeminal neuralgia, especially the less classic features, occur in patients less than 50 years of age, multiple sclerosis should be suspected.¹⁰ Loeser⁷ suggested that the more a facial pain syndrome deviates from the classic criteria, the less likely is primary trigeminal neuralgia (tic douloureux) to be the correct diagnosis.

TREATMENT—As with most clinical pain states whose etiology is only imperfectly understood, treatment of trigeminal neuralgia is often based on theoretical biases of clinicians.

The anticonvulsant drug carbamazepine and the antiepileptic drug phenytoin (Dilantin) have proved especially useful, either as the sole therapy or as an adjunct preoperatively and postoperatively. Carbamazepine is the drug of choice, providing relief in 60% to 80% of cases.

Phenytoin is reported to be effective in 20% of cases. Drug resistance and toxicity, especially to formed blood elements, are the major side effects.

Unfortunately, the optimistic early results reported with carbamazepine as the sole therapy have not been supported by later results. Good to excellent results have been reported for about 70% of patients in the first three months of therapy, but after 3 to 42 months, this drops to 50% of patients.¹¹ Both carbamazepine and phenytoin depress synaptic transmission in the spinal trigeminal nucleus, and drugs with a similar action, especially chlorphenesin (Mao late) and baclofen (Lioresal),⁷ have been used less extensively for the control of trigeminal neuralgia.

Percutaneous radiofrequency trigeminal gangliolysis is one of the safest, most common, least expensive, and most reliable surgical procedures for relief of tic douloureux. Patients retain nearly normal tactile-discriminatory sensory functions.^{7,12} Long-term results show a cure rate of 80%, with complications in less than 5% of cases. The procedure can be performed on the sedated, but not unconscious, patient and is particularly suited to the elderly, debilitated patient, who is a poor surgical risk.

As with most conditions, there is only one trigeminal neuralgia bias.

Decompression of the trigeminal nerve, a surgical procedure of significant advantage in the management of primary trigeminal neuralgia and other approaches to the management of trigeminal neuralgia, have not been supported by later results. Good to excellent results have been reported for about 70% of patients in the first three months of therapy, but after 3 to 42 months, this drops to 50% of patients.¹¹ Both carbamazepine and phenytoin depress synaptic transmission in the spinal trigeminal nucleus, and drugs with a similar action, especially chlorphenesin (Mao late) and baclofen (Lioresal),⁷ have been used less extensively for the control of trigeminal neuralgia.

When the patient is sedated, but not unconscious, the procedure can be performed on the sedated, but not unconscious, patient and is particularly suited to the elderly, debilitated patient, who is a poor surgical risk.

Alternative treatment of trigeminal neuralgia, tic douloureux, blocks with local anesthetic and, rarely, alcohol, the peripheral trigeminal nerve, usually viewed as a last resort, has been attempted. Success is largely

As with most clinical pain states whose etiology is only imperfectly understood, treatment of trigeminal neuralgia is often based on theoretical biases of clinicians.

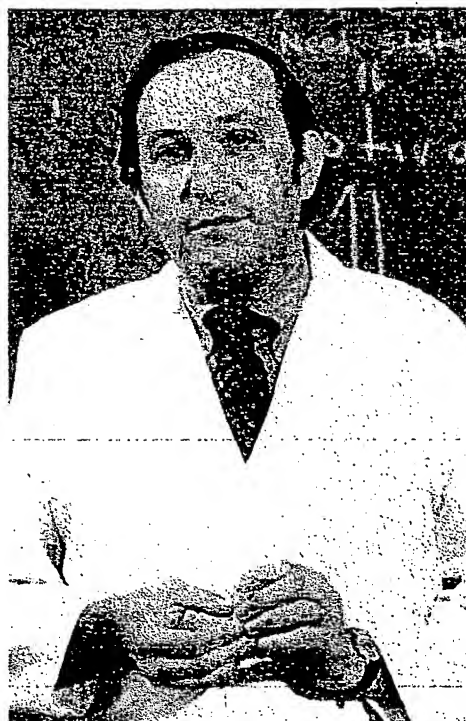
is to be effective. Drug regimens, especially anticonvulsants, are essential. Both carbamazepine and phenytoin are effective, but carbamazepine is preferred because of its lower toxicity. In the absence of response to these drugs, surgical treatment is indicated. Microvascular decompression of the trigeminal nerve is a more invasive surgical procedure, but it is considered a significant advance in the management of primary trigeminal neuralgia and is used when other approaches, notably pharmacotherapy, have failed. Jannetta⁵ devised this microvascular technique to move vascular structures compromising the trigeminal nerve. The great advantage of the technique is that it provides long-term relief without loss of sensation, since nerves are not cut but are repositioned.

When the previously described approaches have failed, trigeminal tractotomy can be performed. The descending trigeminal nerve tract is cut at the cervicomedullary junction. This procedure usually relieves the tic douloureux but causes more general loss of pain and temperature sensations. It is not advocated as an initial procedure and is recommended only with reservation.

Alternative treatments for trigeminal neuralgia, especially for the tic douloureux, include nerve blocks with local anesthetics and, rarely, alcohol injection of the peripheral branches of the trigeminal nerve. These are usually viewed as temporary measures. Acupuncture has been attempted, but its effectiveness is largely unproved. Recently,

trigeminal neuralgia has been successfully treated by retrogasserian glycerol injection, a fairly safe procedure with minimal risk of extensive nerve damage.

POSTTRAUMATIC TRIGEMINAL NEURALGIA—Neuralgia can follow accidental or surgical trauma to the peripheral branches of the trigeminal nerve. In the oral cavity, traumatic neuromas have been described following injuries to inferior alveolar and



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mental nerves and following removal of cysts, impacted third molars, and other teeth.¹² Post-traumatic neuralgia is characterized by stinging, burning, or paresthetic pain of an atypical neuralgic or a nonneuralgic type.

Adequate statistics on the epidemiology of posttraumatic trigeminal neuralgia are not available. Gregg and associates¹³ believe chronic sensory disorders may occur in as many as

continued

TMJ pain-dysfunction syndrome should be considered a family of syndromes rather than a single entity.

one third to one half of patients who have sustained injuries to the inferior alveolar, infraorbital, or lingual nerves.

Treatments that have been tried include transcutaneous nerve stimulation, peripheral neurolysis, and tricyclic antidepressant drugs.¹³ Transcutaneous nerve stimulation is at least temporarily effective for up to 50% of patients but inexplicably aggravates pain in others. However, its benefits outweigh its deficiencies. Peripheral neurolysis appears to be most effective for patients who experience triggered, explosive, paroxysmal pain. Tricyclic antidepressants are effective, although no physiologic explanation is available.

TMJ pain-dysfunction syndrome

TMJ pain-dysfunction syndrome should be considered a family of syndromes rather than a single entity.

ETIOLOGY AND DIAGNOSIS—The most common symptoms of the syndrome are pain on one side of the head, often in the region of the ear and TMJ; limitation of jaw opening; and joint sounds, including crepitus, clicking, and popping. Nonspecific symptoms include headache, disturbances in hearing and balance, and pain radiating to other regions of the face and neck. Pain or tenderness on

palpation of one or more of the muscles of mastication is a reliable finding. Pain often persists for months, years, or even decades,^{13,14} although for many patients, pain is self-limited and lasts less than three months. The syndrome is also called mandibular pain-dysfunction or myofascial pain-dysfunction and is sometimes referred to simply as TMJ.

Epidemiologic studies conducted in many countries indicate that TMJ pain-dysfunction syndrome is on the increase and is affecting younger patients than previously. Earlier reports suggested that the syndrome primarily affected women over 40 years of age; however, a recent study¹⁵ shows that it is equally prevalent in men. The earlier data may have reflected the reluctance of men to seek treatment. In the general population, elicitation of one or more signs of TMJ pain-dysfunction syndrome on examination is more frequent than spontaneous subjective reporting of pain. Some studies^{15,16} have shown that 30% to 50% of subjects had tenderness or pain on palpation, and even higher percentages may have joint sounds that some researchers believe are precursors of TMJ pain-dysfunction syndrome.

The pathophysiology of the syndrome is poorly understood,

continued

Tagamet BRAND OF cimetidine

Before prescribing, see complete prescribing information in SK&F Lab Co. literature. The following is a brief summary.

Indications: Tagamet (brand of cimetidine) is indicated for the short-term treatment of active duodenal ulcer prophylactic use, at reduced dosage, to prevent recurrent duodenal ulcer in patients likely to need surgical treatment such as those with a history of recurrence or complications and those with concomitant illness in whom surgery might constitute a greater than usual risk (limitation to the population is recommended because the consequences of use beyond one year of continuous Tagamet therapy are not known); in the short-term treatment of acute benign gastric ulcer (there is no information concerning usefulness of treatment periods of longer than 8 weeks); and in the treatment of pathological hypersecretion disorders (i.e., Zollinger-Ellison syndrome, systemic mastocytosis and multiple endocrine adenomas). In active duodenal ulcer, concomitant antacids should be given as needed for relief of pain; however, simultaneous administration is not recommended.

Contraindications: There are no known contraindications to the use of Tagamet.

Precautions: In a 24-month toxicity study in rats at dose levels approximately 9 to 56 times the recommended human dose, benign Leydig cell tumors were seen; these were common in both the treated and control groups but the incidence became significantly higher only in the age rats receiving Tagamet.

Rare instances of cardiac arrhythmias and hypotension have been reported following the rapid administration of Tagamet HCl (brand of cimetidine hydrochloride) injection by intravenous bolus.

Symptomatic response to Tagamet therapy does not preclude the presence of a gastric malignancy. There have been rare reports of transient masking of gastric ulcer despite subsequently documented malignancy.

Reversible confusion states have been reported on occasion, predominantly in severely ill patients.

Tagamet has been reported to reduce the hepatic metabolism of warfarin-type anticoagulants, phenytoin, propranolol, chloridazepoxide, diazepam, lidocaine, and theophylline. Clinically significant effects have been reported with the warfarin anticoagulants; therefore, close monitoring of prothrombin time is recommended, and adjustment of the anticoagulant dose may be necessary when Tagamet is administered concomitantly. Interactions with phenytoin, lidocaine and theophylline has also been reported to produce adverse clinical effects.

Lack of experience to date precludes recommendation of Tagamet for use in pregnant patients, women of childbearing potential, nursing mothers or children under 16 years of age. Anticipated benefits outweigh potential risks; general nursing should not be undertaken in patients taking the drug since cimetidine is secreted in human milk.

Decreased white blood cell counts have been reported in Tagamet-treated patients who also received drugs and treatment known to produce neutropenia.

Adverse Reactions: Diarrhea, dizziness, somnolence, headache, rash, mild gynecomastia. Reversible arthralgia, myalgia and exacerbation of joint symptoms in patients with preexisting arthritis have been reported. Reversible confusion states (e.g., mental confusion, agitation, psychosis, depression, anxiety, hallucinations, disorientation) predominantly in severely ill patients, have been reported. Reversible impotence in patients with pathological hypersecretory disorders receiving Tagamet, particularly in high doses, for at least 12 months, has been reported. Reversible alopecia has been reported very rarely. Decreased blood cell counts in Tagamet-treated patients (approximately 1 per 100,000 patients), including agranulocytosis (approximately 5 per million patients), have been reported including a few reports of recurrence on rechallenge. These patients generally had serious concomitant illness and received drugs and/or treatment known to produce neutropenia. Thrombocytopenia (approximately 3 per million patients) and a few cases of aplastic anemia have also been reported. Increased serum transaminase, creatinine, as well as rare cases of liver, interstitial nephritis, hepatitis (occasionally with cholestatic features) and pancreatitis have been reported.

How Supplied: Pale Green Tablets: 200 mg. tablets in bottles of 100; 300 mg. tablets in bottles of 100 and SK&F Packages of 100 (intended for institutional use only). Liquid: 300 mg./5 ml., in 8 fl. oz. (237 ml.) amber bottles.

Injection: 300 mg./2 ml. in single-dose vials and in multiple-dose vials, in packages of 10.

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Among clinicians, the most widely accepted view regarding the etiology of TMJ pain-dysfunction syndrome is that dysfunctional occlusion is a major cause.

and there are numerous etiologic theories. One theory suggests that displacement of the condyle caused by faulty occlusion or muscle hyperactivity may result in inflammation and even in degenerative joint disease, leading to pain and dysfunction.

Pain may be caused by primary joint disease (osteoarthritic changes) resulting in muscle dysfunction. Alternatively, joint disease may be secondary to dysfunction in the musculature or occlusion. Precise radiographic techniques such as cephalometric tomography and arthrography indicate that joint remodeling may occur with condylar displacement.¹⁷

Many investigators strongly disagree that joint disease may play a primary role in TMJ pain-dysfunction syndrome.¹⁵ They argue that the relationship between radiographic evidence of condylar displacement or joint degeneration and TMJ pain is problematic. Laskin and Greene¹⁸ rule out pathologic changes in the TMJ as a criterion for diagnosis of myofascial pain-dysfunction.

The most widely accepted view among clinicians is that dysfunctional occlusion is a major cause of TMJ pain-dysfunction syndrome. For present purposes, dysfunctional occlusion is defined as any kind of premature contact along the oc-

clusal surfaces of the teeth (referred to in dentistry as interference), especially when it affects centric jaw relation or chewing. Disturbing influences from interference alter both mandibular posture and mandibular movement via proprioceptive information from the teeth, periodontium, and alveolar bone and proprioceptive sensory information elicited by condylar movement. Alteration of mandibular posture or mandibular movement causes pain in the joint or muscles.

The term "neuromuscular theory of TMJ pain-dysfunction" has been applied to this interaction of occlusal factors, muscle function, and movement in the joint. This theory maintains that mandibular repositioning must occur because of tooth or occlusal factors and that this in turn leads to maladaptive muscle activity, especially chronic muscle spasm.¹⁶ Few empirical data are available to support this relatively refined hypothesis.

Oral parafunctional disturbances (bruxism, clenching, and other habits harmful to occlusion) are often associated with TMJ pain-dysfunction syndrome. Evidence¹⁹ indicates that bruxism and clenching occur in 15% to 60% of persons with the syndrome. During an eight-hour sleep period, patients with TMJ pain-dysfunction

syndrome who have no clinical evidence of bruxism (ie, facets or extreme abrasion of teeth) spend about twice as much time with their teeth in contact as do normal persons. In patients with clinical evidence of bruxism, however, tooth contact during sleep is seven times that observed in controls.

Psychologic disturbance is considered an important cause of TMJ pain-dysfunction syndrome. Anxiety and stress are especially important, with a long history of mental or emotional disturbance being somewhat less so. Some investigators^{16,20} believe the syndrome is mainly or even exclusively psychogenic, while others^{18,21,22} maintain that psychologic factors are adjunctive or covariant with peripheral factors and that the combination yields the syndrome. The common final pathway by which psychologic factors elicit or maintain pain and dysfunction symptoms is believed to be muscle hyperactivity.

Three methods have been used to study the role of psychologic variables in TMJ pain-dysfunction syndrome: (1) search for relatively enduring aspects of personality (personality trait, perceptual style, or predisposing attitude) that could be related to the syndrome, (2) observation of the degree to which emotional states, especially anxiety,

continued

is Minipress® (prazosin HCl) Capsules 1mg 2mg 5mg

ase I.D. Dosage Convenience

SUMMARY

MINIPRESS® (prazosin hydrochloride) CAPSULES For Oral Use

INDICATIONS: MINIPRESS® (prazosin hydrochloride) is indicated in the treatment of hypertension. As an antihypertensive drug, it is mild to moderate in effect. It can be used as the initial agent or it may be employed in a treatment program in conjunction with a diuretic and/or other antihypertensive drugs as needed for proper patient response.

WARNINGS: MINIPRESS (prazosin hydrochloride) may cause dizziness with sudden loss of consciousness. In most cases this is thought to be due to an excessive postural hypotensive effect; occasionally the syncope has been preceded by a period of severe tachycardia with heart rates of 120-160 beats per minute. Syncope episodes have usually occurred within 30 to 60 minutes of the initial dose of the drug; occasionally they have been reported in association with rapid dosage increases or the addition of another antihypertensive drug into the regimen of a patient taking high doses of MINIPRESS (prazosin hydrochloride). The incidence of syncope episodes is approximately 1% in patients on an initial dose of 2 mg or greater. Clinical trials conducted during the investigational phase of this drug suggest that syncope can be minimized by limiting the initial dose of the drug to 1 mg; by subsequently increasing the dosage slowly, and by adding any additional antihypertensive drugs into the patient's regimen with caution (see DOSAGE AND ADMINISTRATION). Syncope may develop in patients taking MINIPRESS who are also taking a beta-blocker such as propranolol.

If syncope occurs, the patient should be placed in the recumbent position and supported as necessary. This adverse effect is self-limiting and does not recur after the initial period of therapy or during subsequent dose titration.

Patients should always be started on the 1 mg capsules of MINIPRESS (prazosin hydrochloride). The 2 and 5 mg capsules are not indicated for therapy.

More common than loss of consciousness are the symptoms often associated with lowering of the blood pressure, namely, dizziness and weakness. The patient should be cautioned about these possible effects and advised what measures to take should they develop. The patient should also be cautioned to avoid situations where injury could result from syncope occurring during the initiation of MINIPRESS (prazosin hydrochloride) therapy.

Use in Pregnancy: Although no teratogenic effects were seen in animals, the safety of MINIPRESS (prazosin hydrochloride) in pregnancy has not been established. MINIPRESS (prazosin hydrochloride) is contraindicated in pregnant women unless the potential benefit outweighs the risk to mother and fetus.

Use in Children: No clinical experience is available with the use of MINIPRESS (prazosin hydrochloride) in children.

ADVERSE REACTIONS: The most common reactions associated with MINIPRESS (prazosin hydrochloride) therapy are: dizziness 10.3%, weakness 7.6%, drowsiness 7.6%, lack of energy 6.9%, weakness 6.5%, fatigue 5.3%, and nausea 4.9%. In most instances side effects have occurred with continued therapy or have been tolerated with no decrease in drug effect.

Following reactions have been associated with MINIPRESS (prazosin hydrochloride), some of them rarely. (In some instances exact causal relationship has not been established.)

Central Nervous System: nervousness, vertigo, depression, paresthesia, headache, rash, pruritus, alopecia, lichen planus.
Genitourinary: urinary frequency, incontinence, impotence, priapism.
Eyes: blurred vision, reddened sclera, epistaxis, tinnitus, dry mouth, lacrimation.
Cardiovascular: eczema, dyspnea, syncope, tachycardia.

Other: reports of pigmentary mottling and serous retinopathy, and a few cases of cataract development or disappearance have been reported. In all instances, the exact causal relationship has not been established. The baseline observations were frequently inadequate. More specific slit-lamp and funduscopic studies, which included baseline examinations, no drug-related abnormal ophthalmological findings have been reported.

DOSE AND ADMINISTRATION: The dose of MINIPRESS (prazosin hydrochloride) should be adjusted according to the patient's individual blood pressure response. The following is a guide to its administration:

Initial Dose: 1 mg two or three times a day. (See Warnings.)

Maintenance Dose: Dosage may be slowly increased to a total daily dose of 15 mg given in divided doses. The therapeutic dosages most commonly used have ranged from 6 mg to 15 mg daily given in divided doses. Higher than 20 mg usually do not increase efficacy, however a few patients benefit from further increases up to a daily dose of 40 mg given in divided doses. After initial titration some patients can be maintained on a twice daily dosage regimen.

With Other Drugs: When adding a diuretic or other antihypertensive drug to the dose of MINIPRESS (prazosin hydrochloride) should be reduced to 1 mg two or three times a day and retitration then carried out.

SUPPLIED: MINIPRESS (prazosin hydrochloride) is available in 1 mg (#431), 2 mg (pink and white #437) capsules in bottles of 250, 1000, and unit dose institutional packages of 100 (10 x 10's); and 5 mg (blue and white #438) capsules in bottles of 250, 500 and unit dose institutional packages of 100 (10 x 10's).

Additional information available on request.



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Psychologic disturbance, especially anxiety and stress, are considered important causes of TMJ pain-dysfunction syndrome.

stress, depression, anger, and frustration, are present in patients with the syndrome, and (3) use of learning theory and behavior modification techniques. Few studies have explored the relationship between depression and TMJ pain-dysfunction syndrome. Since depression is acknowledged to play a prominent role in other chronic pain states, lack of information regarding its role in TMJ pain is surprising.

Rugh and Solberg²⁰ summarized the best available studies of personality recorded from different theoretical perspectives. No single personality trait or cluster of traits forming a personality profile emerged from these data. Moreover, it has not been demonstrated whether certain personality traits cause TMJ pain-dysfunction syndrome or result from it.

Studies demonstrating elevated levels of 17-hydroxycorticosteroid and adrenergic metabolites in the urine provide evidence that some patients with TMJ pain-dysfunction syndrome may be under stress. However, the relationship between stress and this syndrome has not been carefully studied.

TREATMENT—Most therapeutic approaches to TMJ pain-dysfunction syndrome involve education and reassurance, followed by some form of modification of

pathologic patterns of muscle function and joint articulation (eg, use of removable bite guards, adjustment of the occlusion). Biofeedback and other methods of behavior modification have been used to modify muscle function or eliminate parafunctional habits and thus reduce pain and restore function. Some reports indicate that use of electromyographic biofeedback from the muscles of mastication has provided relief for 60% to 90% of patients.²⁰ However, it appears that the benefits may reflect changes in the patient's perception of pain during relaxation as much as they reflect changes in electromyographic levels.

Surgical approaches derive from the view that degenerative joint disease or pathologic joint remodeling causes TMJ pain-dysfunction syndrome. Discectomy and condylectomy seem to be the most common procedures; reports of their use have increased dramatically over the past decade. The immediate benefits are decrease in pain and increase in function, but controlled studies with follow-up are not yet available. Muscle relaxants and antiinflammatory nonnarcotic analgesics are the drugs most commonly used for treatment of TMJ pain, but reports of success are difficult to evaluate.

continued

Some chronic pain patients may be resistant to all the previously described therapies. Psychologic referral is viewed as a last resort by many clinicians who are frustrated by the failure of mechanical or surgical approaches. However, psychologic referral as a last resort seems less effective than early psychologic consultation.

Results of treatment are often reported after several therapies have been instituted, so that effects of individual pharmacologic, mechanical, and surgical treatments cannot be quantified. Clinicians and researchers interested in behavior changes of patients with pain have observed that all forms of psychotherapy enhance the pharmacologic, surgical, and psychophysiological treatments of chronic pain. Multidisciplinary pain clinics, by definition, function on just such an assumption of interdependency. However, the management of TMJ pain-dysfunction syndrome does not yet appear to be as systematically multidisciplinary as the management of other general pain syndromes.

Summary

Trigeminal neuralgia and temporomandibular joint (TMJ) pain-dysfunction syndrome are the most common benign oro-

facial pain disorders. Because orofacial pain can arise from many sources and can be exacerbated by emotional stress, diagnosis is complex.

Primary trigeminal neuralgia (tic douloureux) is characterized by severe paroxysms of pain often initiated by stimuli applied to trigger zones. Atypical facial neuralgia is a more loosely defined collection of orofacial neuralgias with variable distribution of pain and age of onset. Treatment (ie, pharmacologic and surgical procedures, nerve blocks, alcohol injection) is often based on the theoretical biases of

clinicians.

The most common clinical findings in TMJ pain-dysfunction syndrome are localized facial pain, mandibular dysfunction, and joint sounds. Therapy includes use of drugs to relieve pain and relax muscles, elimination of occlusal discrepancies, and surgical procedures. Psychologic referral is usually considered a last resort. JGFM

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THE MEDICAL MANAGEMENT OF MASSETERIC HYPERTROPHY WITH BOTULINUM TOXIN.

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SUMMARY

The authors present a series of cases of masseteric hypertrophy with associated muscular facial pain treated with botulinum toxin.

INTRODUCTION

Masseteric hypertrophy is an uncommon condition which presents as swelling of the masseter muscle. It may be unilateral or bilateral. Pain is usually not a feature. Traditionally masseteric hypertrophy has been managed surgically with significant morbidity particularly the occurrence of post-operative trismus^{1,2}. Recent papers have demonstrated the successful use of botulinum in the treatment of masseteric hypertrophy^{3,4}. We present a series of cases of masseteric hypertrophy in which pain was also a feature. Treatment with botulinum toxin not only corrected the facial appearance but also eliminated the associated facial pain. No side effects of treatment were encountered.

CASE REPORTS

Case 1

A 22 year old single female was referred to the oral surgery department of Cork Dental Hospital complaining of swelling bilaterally at the angles of her mandible. These swellings were associated with pain and tenderness and had been present for about six months. Clinical

examination revealed that the swellings corresponded to the outline of the masseter muscles and became exaggerated on clenching (Fig 1). Both muscles were tender to palpation. After discussing treatment options with the patient it was decided to attempt reduction of the muscle mass by injecting botulinum toxin. On review over the subsequent two months pain had resolved and no adverse effects of treatment was reported. The degree of atrophy was somewhat greater on the right side and a second injection was made on this side. The facial appearance became symmetrical and the patient remains free of swelling and pain eighteen months after treatment (Fig 2).

Case 2

A 31 year old married woman was referred by her dentist with a two year history of left sided localized swelling and pain at the left angle of her mandible (Fig 3). The pain was described as a "tightness" which was episodic but frequent. A diagnosis of masseteric hypertrophy was made and the muscle was injected with botulinum toxin. The swelling began to decrease after two weeks and at five weeks the facial appearance became symmetrical (Fig 4). Significantly, the pain associated with the hypertrophied muscle cleared up completely and the patient has remained pain free one year after treatment.

Case 3

A 48 year old housewife complaining of left sided facial swelling and pain of approximately six months duration was referred to the Oral Surgery Department. The patient's primary concern was with the appearance of her face. Masseteric hypertrophy was

diagnosed and this was treated with botulinum toxin. On review at two months the left sided swelling had decreased to give a normal facial appearance. All pain had resolved. No side effects were reported.

Case 4

A 19 year old waitress was referred by her general dental practitioner with swelling at the left angle of her mandible. She became aware of this swelling 18 months previously after extraction of her left lower wisdom tooth. There was no associated pain. The young woman was concerned with her facial appearance and requested treatment. The left masseter was injected with botulinum toxin and at review two months later the swelling had resolved and no adverse effects were reported.

TECHNIQUE

One vial of botulinum toxin type A (Dysport) contains 500 units of the toxin. The drug is formulated as a powder and is made up to 2.5mls with normal saline. Each millilitre contains 200 units of botulinum toxin. The toxin needs to be injected into the bulkiest portion of the swelling. For larger swellings more than one injection site may be used. A 25 gauge needle is inserted down to bone and withdrawn into the muscle mass to ensure deposition in the correct location. A maximum of 200 units (1 ml) is injected at each side (0.5 mls at each separate site). Self limiting dysphagia is the only significant side effect that has been reported.⁵

DISCUSSION

Masseteric hypertrophy was first described in 1880 by Legg⁶. It is

manifest as a slowly enlarging swelling of the lower and posterior parts of the face caused by chronic hypertrophy of the masseter muscle.⁷ In the majority of cases the exact aetiology is unclear⁸ and is most likely to be multifunctional⁹. The main concern of the patient is usually facial deformity¹⁰. Pain is not usually a feature.

Palpation of the clenched muscle reveals that the swelling lies within the masseter muscle and its texture is identical to that of the surrounding muscle. Complicated and expensive investigations such as CT and MRI are unnecessary and diagnosis of the condition is essentially clinical.

Treatment is directed toward the correction of the facial appearance. Conventional treatment approaches have been both surgical and medical. Medical treatment include spasmolytics, benzodiazepines and occlusal equilibration⁹. With all these approaches results have been poor. Until recently the accepted approach to treatment of the aesthetic problem relied on surgical reduction of the mass of the muscle bulk. Extraoral¹¹ and intraoral^{1,2,9} surgical techniques have been described. The extraoral approach results in a scar and the risk of damage to the mandibular branch of the facial nerve. The intraoral approach is technically difficult because of restricted access². Both approaches result in the disadvantages of considerable morbidity, marked trismus and poor aesthetic outcome¹.

Botulinum toxin type A is a protein neurotoxin elaborated by the anaerobic bacillus *Clostridium botulinum*. The toxin exerts its paralytic action by irreversibly binding to presynaptic cholinergic receptors inhibiting the secretion of acetylcholine^{1,2}. This gives rise to loss of junctional acetylcholine receptors, in effect chemodenervating the muscle. Botulinum toxin has been used

successfully in the treatment of blepharospasm and hemifacial spasm,^{13,14,15} cervical dystonia^{16,17}, hyperkinetic facial lines^{18,19}, torticollis²⁰, and masseteric hypertrophy^{3,4}. No reports of resolution of facial pain have been reported.

The resolution of muscle pain in three of the four cases presented in this series is noteworthy. The muscle and joint pain of Temporomandibular Joint Dysfunction is usually attributable to increased activity of the masticatory muscles resulting from parafunctional habits such as bruxism. It may be that treatment with botulinum toxin may prove beneficial in the treatment of facial pain of muscular origin secondary to overactivity and which fails to respond to conservative management.

CONCLUSION

It is clear that the use of botulinum toxin represents a significant advance in the treatment of masseteric hypertrophy. We believe that surgical treatment should now be considered as a second line option and that the risks of surgery far outweigh those of the pharmacologic approach. Furthermore, in the cases presented here the resolution of facial pain may indicate a role for the use of botulinum toxin in the treatment of facial pain secondary to overactivity of the masticatory muscles.

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Case 1: Facial appearance at presentation.



Case 1: Facial appearance after treatment with Botulinum.



Case 2: Left sided masseteric hypertrophy.



Case 2: Facial appearance 5 weeks after treatment.

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1. AU Wang A.; Jankovic J.
CS Dr. J. Jankovic, Movement Disorders Clinic, Department of Neurology,
Baylor College of Medicine, 6550 Fannin, Houston, TX 77030, United States
SO Muscle and Nerve, (1998) 21/12 (1740-1747).
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Review Article

Headache Management in an Interventional Pain Practice

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More than 20 million people in the United States suffer from severe headaches. Most have been diagnosed as migraines, which have been assumed to be an intracranial process. Recognition of the extracranial sources of headaches (such as supraorbital neuralgia, infraorbital neuralgia, auriculotemporal neuralgia, facial neuralgia, posterior auricular neuralgia, occipital neuralgia, cervical facet pathology, masseter spasm, sternocleidomastoid muscle spasm, trapezius spasm, and interspinous ligament pathology) has

led to an expansion of the treatment options available for practitioners skilled in interventional pain procedures. However, unless the clinical presentation is recognized, treatment cannot be offered. Clinical presentation, diagnostic injections, differential diagnosis, and advanced neurolytic techniques are discussed in this article.

Keywords: Headache, migraine, facial neuralgia, neurolysis

More than 20 million people in the United States suffer from severe headaches, and the annual prevalence has increased nearly 60% since 1980. Nearly 80% of these patients report headache-related disability that may result in missed work. In fact, nearly 50% of headache sufferers are moderately or severely disabled by a headache attack or "migraine" and lose an estimated thirteen workdays and eight leisure days each year (1).

Migraine is a term of much confusion in the lay public's mind. Physicians, especially neurologists, use the term migraine to mean a specific intracranial vascular headache. Patients usually use the term to mean a "sick headache" or a throbbing headache. Pain management doctors treating headache patients are beginning to realize that the symptomatic diagnosis of migraines (unilateral throbbing headache associated with photophobia, phonophobia and emesis) does not distinguish between intracranial and extracranial causes of headaches.

In this article I will discuss some of the most common causes we have found to be associated with "migraines" and intractable headaches.

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SUPRAORBITAL NEURALGIA

Entrapments of the first-division of the trigeminal nerve can cause unilateral or bilateral throbbing headaches, often just before menses or triggered by bright lights that cause squinting. Supraorbital neuralgia can be mistaken for frontal sinusitis. It can be caused by trauma to the face, such as when the head hits the windshield or after a punch to the face. The headache might not present for many years until the scar cicatrix tightens enough around the nerve to finally cause entrapment. There can be auras and unilateral or bilateral throbbing, as well as photophobia, phonophobia, nausea and vomiting; and these headaches can meet all the International Headache Society (IHS) criteria for migraines. Fluid retention, such as before menses or with salt indiscretion (perhaps with red wine, monosodium glutamate, or cheeses) can trigger these "migraines." The supratrochlear nerve is also in this region and can be injured by poor-fitting eyeglasses, presenting as a more midline forehead pain. We have also seen patients with "classic" cluster headaches (men, sudden onset, rhinorrhea, scleral injection, cyclic pattern) who have had instant and complete relief of their headaches with injection of small (0.5 cc volume) of local anesthetic.

Treatment (and diagnosis) involve injection of local anesthetic with steroid, preferably during the headache initially. Small volumes need to be used to avoid increasing the entrapment, and it has been dramatic how the headache resolves "almost before the needle is out," with rapid relief

of the nausea, photophobia, and other associated symptoms.

Cryoneurablation can give long-term relief by freezing the nerve at the supraorbital notch. Plastic surgeons using Botox for forehead wrinkles noted a dramatic decrease in "migraines" in treated patients, suggesting that muscle entrapment of the supraorbital and supratrochlear nerves may be a common pathology. Topical anti-inflammatory agents can also be very useful because of the thinness of the skin in this area.

INFRAORBITAL NEURALGIA

This second division of the trigeminal nerve is also associated with headaches, often misdiagnosed as maxillary sinusitis. Like the supraorbital nerve, it can be injured years before the headaches start and can present as menstrual headaches or classical/common migraines. The diagnosis is again made by injection, preferably during the headache; and cryoneurablation (intraoral or extraoral) can be used.

AURICULOTEMPORAL NERVE

Temple headaches are often due to entrapment of the auriculotemporal nerve, a third-division trigeminal nerve that leaves the foramen ovale and then travels in front of the temporomandibular joint (TMJ) (enervating the joint as it goes by) to pierce the temporalis muscle. This is a common headache site (visualize all the headache patients rubbing or pressing their temples for relief). Patients will awaken with a headache at three or four o'clock in the morning secondary to bruxism during the lightest plane of sleep, ie early in the morning. The headache can be unilateral or bilateral and throbbing in nature because of the proximity of the temporal artery. In fact, tenderness of the "temporal artery" has been used as supporting evidence of the vascular nature of migraines instead of recognizing that the auriculotemporal nerve is possibly the true pathology. Teeth clenching with stress, prolonged talking or chewing and "TMJ" pathology (which may be actually auriculotemporal nerve irritation) can all trigger these headaches.

The relief seen with injection of the nerve during a migraine "attack" can be dramatic and gratifying and patients have gone back to work a half hour after "throwing up my toenails." Bite blocks, sleep aids, and topical anti-inflammatories are usually curative; and cryoneurablation and Botox have been used successfully in recalcitrant cases.

ZYGOMATIC FACIAL NERVE

Although the facial nerve is usually considered a pure motor nerve, there are sensory fibers across all the branches. The most common entrapment site we see is the zygomatic branch as it crosses the zygomatic arch. Edentulous patients will have the coronoid process move cephalad, which catches the nerve in the arch. The pain can mimic the pattern seen by either the auriculotemporal nerve or maxillary nerve. The headache may be worse in the early morning after the dentures have been removed the night before and the body tries to "find" the previous "natural" site of dental occlusion. These usually respond to injection therapy but cryoneurablation may be needed.

POSTERIOR AURICULAR NERVE

Ear pain and parietal headaches can be caused by entrapment of the posterior auricular nerve by the sternocleidomastoid muscle. This can occur during flexion/extension injuries, especially if the head was turned at impact. Blows to the side of the head can also present as posterior auricular entrapment years later. There can be persistent "fullness" in the ear or decreased hearing, as well as tinnitus and vertigo. These symptoms may be difficult to differentiate from sternocleidomastoid pathology (see sternocleidomastoid). Injections need to be of a small volume. Cryoneurablation can be used with caution, noting the very thin skin and the ease with which the probe could slide off the skull into the carotid sheath.

GREATER AND LESSER OCCIPITAL NERVE

The occipital nerve is made up of the dorsal rami of C2 and C3 (see cervical facets) (2). Classic occipital neuralgia causes pain in the back of the head. However, because the ganglion interconnects with the trigeminal ganglion in the brain stem (3), occipital neuralgia will refer to any of the branches of the trigeminal nerves, especially the retroorbital area. These nerves pierce the nuchal fascia at the base of the skull and are therefore prone to trauma from flexion/extension injuries, as well as entrapment by spasm of the trapezius muscle. There is a frequent association with throbbing (because of the proximity of the occipital artery), as well as nausea and vomiting. If the head was turned at impact, there would be a unilateral pain, which would then meet IHS criteria for migraines. There is usually also temporary relief with "triptans," presumably because the occipital artery is constricted by the medicine, temporarily reducing the entrapment of the occipital nerve. However, as soon as the medicine wears off (usually about six to

eight hours), the headache comes right back. A prospective study of patients presenting to the emergency department (4) with unilateral occipital headaches found that 42% of the patients complained of nausea, 50% of dizziness, and 33% of tinnitus, with visual disturbances in 67%.

Standard anesthesia texts recommend injecting large volumes (10 cc) at the nuchal ridge in a "fan" fashion. However, this large a volume of fluid will cause an entrapment, and the nerve pathology is more caudad so that the medicine does not reach the area of injury. The injection technique I recommend identifies the injection site (in this case describing the right side) by placing the thumb of the right hand at the foramen magnum (which identifies midline and avoids cisternal injections); the index finger is placed at the conjoined tendon attachment, and the second finger identifies the injection site at the base of the skull. Small volumes (less than 2 cc) of local and steroid are thereby injected underneath the tendon where the nerve pierces the tendon. Cryoneurablation is performed at the same site.

Recent reports suggest that stimulation of the occipital nerve using a spinal cord stimulator lead placed subcutaneously can provide relief of intractable occipital headaches (5).

CERVICAL FACET PATHOLOGY

Although cervical facet pathology can obviously cause neck pain, the upper cervical facets are enhanced by the dorsal rami that make up the occipital nerves (6). Therefore, C2 and C3 facet pathology will refer to the occipital nerve. In a similar way, pathology of the cervical discs can cause cervicogenic headaches. This is a common cause of headaches in the elderly because of the predominance of cervical arthritis. However, flexion/extension injuries will also cause cervical facet pathology, unilateral if the head was turned on impact (7). Cervical facet blocks can diagnose, as well as treat these headaches. Cryoneurablation and radiofrequency lesions of the cervical facets can be very useful for longer-term relief. Cervical intradiscal electrothermal coagulation may offer relief if the technique is expanded to the cervical region.

MASSETER MUSCLE

Chronic stress leading to teeth clenching, bruxism, dental malocclusion, and TMJ pathology can all cause spasm of the masseter muscle, which will refer pain to the temples and jaw, and over the eye (8). Local anesthetic injections

are diagnostic and therapeutic. Neuromuscular therapy can be useful and Botox can be used with care.

STERNOCLEIDOMASTOID MUSCLE

This muscle will refer pain to the ear, temple and face, especially over the eye (8). Patients often complain of fullness in the ear with decreased hearing, leading to unnecessary ear, nose and throat evaluations. There can also be tinnitus and vertigo, mimicking vestibulitis. Since flexion/extension injuries will traumatize the sternocleidomastoid, what have been considered coup-contrecoup brain injuries are now being recognized as myofascial pain. Posterior auricular neuralgia can be caused by sternocleidomastoid entrapment or can mimic the condition. The sternocleidomastoid muscle can also mimic supraorbital neuralgia, auriculotemporal neuralgia, or masseter spasm. Injections of local anesthetic are diagnostic and therapeutic, and Botox may be useful.

TRAPEZIUS MUSCLE

Tension headaches is a term that seems to trivialize the intractable occipital and retro-orbital headaches that are caused by trapezius spasm (8). The pain can be caused by stress, chronic postural problems (for instance with prolonged neck flexion for reading), or flexion/extension injuries. The muscle can entrap the occipital nerve or refer in a similar pattern. These headaches often start as a dull ache in the neck but can refer sharp, stabbing pain to the retro-orbital region. Trigger-point injections are diagnostic and therapeutic and Botox has been quite useful.

INTERSPINOUS LIGAMENT

In 1954, Feinstein and colleagues (9) followed-up on work done by Kellgren (10) in 1939, which showed that irritation of the cervical ligaments can refer pain to the head and face as well as the extremities. These cervical ligaments are traumatized in flexion/extension injuries but this also can occur with chronic low-grade trauma. The subsequent ligament laxity no longer allows support of the 30-lb head and the cervical muscles will go into spasm to hold the head up. This ligament pathology results in a straightening of the cervical lordosis. Thus, the common X-ray diagnosis of "loss of cervical lordosis secondary to spasm" is actually the reverse-contraction of a muscle above and below the lordosis must cause more lordosis if the muscles are the pathology.

Prolotherapy (or reconstructive therapy or stimulated ligament repair) can very effectively restore the ligament, thereby "taking up the slack," which then removes the mechanical pathology causing the trapezius spasm and occipital neuralgia. Radiofrequency lesioning of the fibro-osseous junction at the spinal process has also proved to be useful.

In conclusion, many of the assumptions we have made regarding headaches and migraines are changing. This has important implications for the patient since extracranial headaches do not respond to standard intracranial treatment. Instead, diagnosis is made by palpation followed by injection of local anesthetic. Treatment is directed at reversing the underlying pathology, so that entrapments are treated with injectable anti-inflammatories, muscle spasms treated with muscle relaxants or possibly Botox, and ligament pathology treated with stimulated ligament repair. Cryoneuroablation, radiofrequency lesioning, disc annuloplasty, and subcutaneous nerve stimulation are all now being used with good success for chronic intractable headaches. The interventional pain physician is in a unique position to radically improve patients' lives. The axiom, "you can't treat what you can't diagnose," has never been more true than in the treatment of headaches and migraines.

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